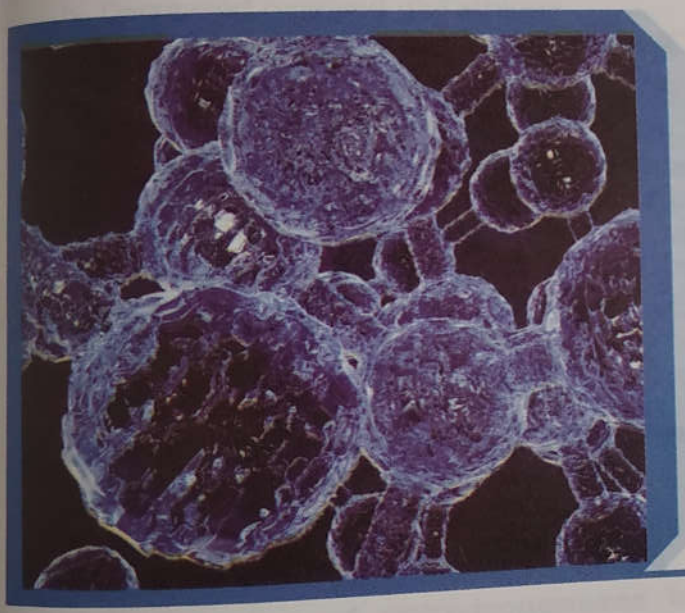


BIOCHEMISTRY

Carbohydrate Chemistry and Metabolism – Questions

Q1: Vitamin C cannot be produced in humans due to lack of:

a. L-gulonolactone oxidase
b. Xylutitol reductase
c. Pyruvate dehydrogenase
d. UDP glucose dehydrogenase

Q2: Why does hemolysis occur in G6PDdeficiency?

a. 6-phosphogulonolactone not formed
b. Decreased oxidised glutathione
c. Accumulation of free radicals in RBC membrane
d. Due to methemoglobin formation

Q3: A lady developed severe hyperglycemia in pregnancy and it returned to normal after pregnancy with history of same in her mother and sister. What is the enzyme defect?

a. Glucokinase
b. PFK
c. Aldolase
d. Enolase

Q4: Erythrocyte glutathione reductase deficiency is seen in deficiency of:

a. Riboflavin
b. Folicacid
c. VitaminC
d. VitaminE

Q5: Total number of dehydrogenases in Kreb's cycle:

a. 3
b. 2
c. 4
d. 5
d. 5

Q6: Which of the following yields 3 molecules of ATP under anaerobic metabolism?

a. Glucose
b. Galactose
c. Glycogen
d. Amino acid

Q7: A patient's CSF fluid analysis shows a CSF glucose of 30. His CSF/Plasma glucose ratio is 0.4. Which of the following GLUTs transports glucose in brain?

a. 1 and 2
b. 3 and 4
c. 2 and 3
d. 1 and 3

Q8: Enzyme catalysing substrate level phosphorylation in TCA cycle:

a. Fumarase
b. Succinate dehydrogenase
c. Succinate thiokinase
d. Alpha ketoglutarate dehydrogenase

Q9: The number of high energy bonds required to get 1 molecule of glucose from 2 molecules of lactate in anaerobic metabolism is:

a. 4
b. 8
c. 6
d. 12

Q10: Major factor that determines if glucose is oxidized by aerobic or anaerobic glycolysis is:

a. NADH
b. FADH2
c. Presence of mitochondria
d. Presence of low glucose

Q11: Which of the following enzyme activity decreases in fasting?

a. Hormone sensitive lipase
b. Glycogen Phosphorylase
c. Acetyl CoA Carboxylase
d. Phosphofructokinase I

Q12: An adolescent male patient came with pain in calf muscles on exercise. On biopsy excessive amount of glycogen present was found to be present in the muscle. What is the most likely enzyme deficiency?

a. Muscle debranching enzyme
b. Phosphofructokinase I
c. Glucose-6 phosphatase
d. Phosphorylase enzyme

Q13: Fluoride released from fluoroacetate inhibits which metabolic pathway?

a. TCA cycle
b. Glycolytic pathway
c. Oxidative phosphorylation
d. ETC

1. a	2. c	3. a	4. a	5. c	6. c	7. d	8. c	9. c	10. c
11. d	12. d	13. a							

Q14: Insulin dependent glucose transport occurs in which of the following tissues?

a. Kidney
b. Adipose tissue
c. Liver
d. Brain

Q15: Which of the following mucopolysaccharide does not contain an acidic sugar?

a. Chondroitin sulfate
b. Keratin sulfate
c. Dermatan sulfate
d. Heparin

Q16: Carbohydrate moiety of Antigen recognizing site in RBC used for blood grouping is:

a. Fucose
b. Xylulose
c. Arabinose
d. Xylose

Q17: Glycolysis is/are regulated by:

a. Hexokinase
b. Pyruvate kinase
c. Phosphofructokinase
d. Glucose 1, 6 bisphosphatase
e. Pyruvate dehydrogenase

Q18: Which of the following is/are reducing sugar(s):

a. Glucose
b. Isomaltose
c. Sucrose
d. Galactose
e. Trehalose

Q19: Uridine diphosphoglucose (UDPG) help in:

a. Galactose synthesis
b. Glycogen synthesis
c. Bilirubin metabolism
d. Ganglioside synthesis
e. Heparin synthesis

Q20: True regarding Krebs cycle:

a. Pyruvate condenses with oxaloacetate to form citrate
b. Alpha keto-glutarate is a five carbon molecule
c. Oxidative phosphorylation occurs within the cytoplasm
d. Krebs cycle functions under anerobic conditions

Q21: NADPH is generated in the reaction catalyzed by:

a. LDH
b. G6PD
c. G3PD
d. Alcohol dehydrogenase

Q22: Glucose transported involved in insulin stimulate glucose transport is GLUT:

a. 1
b. 2
c. 3
d. 4

Q23. Anaerobic glycolysis occurs in all except:

a. RBCs
b. Lens
c. Brain
d. Testis

Q24. Which of the following metabolites involve glycogenolysis, glycolysis and Gluconeogenesis?

a. Galactose-1-phosphate
b. Glucose-6-Phosphate
c. Uridine diphosphoglucose
d. Fructose-6-phosphate

Q25: Final product in anaerobic glycolysis

a. Pyruvate
b. Acetyl CoA
c. Lactate
d. Oxaloacetate

Q26. True regarding Gluconeogenesis requiring Pyruvate is

a. Biotin is required
b. Glucagon is an inhibitor
c. Lactate is essential intermediate
d. Occurs in cytoplasm

Q27. PFK-1 inhibitor:

a. AMP
b. Citrate
c. Glucose 6 phosphate
d. Insulin

Q28. All are used in gluconegenesis except:

a. Oleate
b. Succinate
c. Glutamate
d. Aspartate

Q29. Glucose is transported in pancreas through which receptor

a. GLUT 1
b. GLUT 2
c. GLUT 3
d. GLUT 4

14. b	15. b	16. a	17. a,b,c	18. c,e	19. all	20. b	21. b	22. d
23. c	24. b	25. c	26. a	27. b	28. a	29. b		

Q30. Which reaction uses propionic acid?

a. Glycolysis
b. Gluconeogenesis
c. Glycogenolysis
d. None

Q31. The energy for glycogenesis is provided by

a. GTP
b. GDP
c. UTP
d. AMP

Q32. HMP shunt is of great importance in cellular metabolism because it produces

a. ATP
b. ADP
c. Acetyl CoA
d. NADPH

Q33. Which of the following is not a product of HMP shunt?

a. NADPH
b. D fructose 6 Phosphate
c. D sedoheptulose 7 Phosphate
d. D glyceraldehydes 3 Phosphate

Q34. cAMP increases glycogenolysis by:

a. Contributing phosphate
b. Causing deposphorylation
c. Uncoupling
d. All of the above

Q35. Enzyme that hydrolyzes sucrose is:

a. Invertase
b. Amylase
c. Emulsen
d. Sucrose phosphorylase
e. Saccharase

Q36. An enzyme not involved in glycolysis is

a. Enolase
b. Phosphoglyceromulase
c. Aldolase
d. Glycerophosphate dehydrogenase

Q37. Within the RBC, hypoxia stimulates glycolysis by which of the following regulating pathways

a. hypoxia Stimulates pyruvate dehydrogenase by increased 2,3 DPG
b. Hypoxia inhibits hexokinase
c. Hypoxia stimulates release of all Glycolytic enzymes from band 3 on RBC membrane
d. Activation of the regulatory enzymes by high pH

Q38. All the following gluconeogenic except:

a. Glycerol
b. Alanine
c. Acetoacetate
d. Lactate

Q39. First committed step in Glycolysis is

a. Hexokinase
b. Glucokinase
c. Phosphofrutokinase
d. Aldolase

Q40. Key glycolytic enzymes

a. Phosphofructokinase
b. Hexokinase
c. Pyruvate kinase
d. Glucose 1.6 diphosphatase

Q41. Enzymes in glycogen metabolism

a. Phophorylase a
b. Phosphoylase b
c. Glycogen Synthase I
d. Glycogen Synthase C
e. Branching enzyme

Q42. Hexose monophosphate shunt occurs in all except:

a. Liver
b. Adipose tissue
c. Mammary gland
d. Skeletal muscle
e. Skin

Q43. Skeletal muscle is deficient in

a. Glucose 6 phosphatase
b. Hexokinase
c. Isomerase
d. Phosphofructokinase

Q44. Oxaloacetate + Acetyl CoA + H2O = Citrate + CoA This is an example of

a. Hydration
b. Deacylation
c. Dehydrogenation
d. Condensation

Q45. Glycogen synthetase is increased by-

a. Cortisone
b. Insulin
c. Lactate
d. Ethanol

30. b	31. c	32. d	33. c	34. a	35. a	36. d	37. c	38. c
39. c	40. a,b,c	41. a	42. e d	43. a	44. d	45. b		

Q46. About Galactose which is true:

a. Has the same molecular weight as glucose
b. Is directly converted to glucose by the enzyme galactose oxidase
c. Is liberated when lactose is hydrolysed
d. From the diet is stored in the liver as galactose I-phosphate
e. In the urine gives a positive test with clinitest tablets

Q47. Dehydrogenases of HMP shunt are specific for

a. FAD b. NAD
c. NADPH d. FMN

Q48. Blood glucose levels cannot be augmented by mobilization of muscle glycogen due to lack of

a. G-6-P dehydrogenase
b. G – 6-phosphatase
c. Adolase
d. Glucokinase

Q49. UDP glucose is converted to UDP-glucuronic acid by

a. ATP b. FAD
c. NAD d. NADP

Q50. The sugar component cerebrosides is :

a. Fructose b. Sucrose
c. Galactose d. Glucose

Q51. Reducing sugar in urine is seen in:

a. Fanconi anemia
b. Lactose intolerance
c. Galactosemia
d. Phenylketonuria
e. Salicylate poisoning

Q52. Phosho-dephosphoylation of phosphofructokinase and fructose 1, 6 Biphosphatase by fructose 2, 6 Biphosphate regulations is seen in

a. Brain b. Liver
c. Adrenal Cortex d. RBC
e. Muscle

Q53. Reducing ability of a carbohydrate is due to presence of

a. A hemiacetal
b. Cupric ions
c. A free carboxy
d. A free hydroxyl

Q54. Positive signals for glycogen breakdown include in all the following except:

a. Cyclic AMP b. Blood glucose
c. Epinephrine d. Calcium

Q55. First substrate of Kreb's cycle is :

a. Pyruvate b. Glycine
c. HCL d. Lipoprotein

Q56. What is the substrate for the only physiologically irreversible reaction in the Krebs citric acid cycle:

a. Citrate
b. Alpha ketoglutarate
c. Succinate
d. Malate

Q57. How many ATPs are formed in the TCA cycle from acetyl coenzyme A (one molecule)

a. 10 b. 11
c. 12 d. 15

Q58. Carbohydrate protein and fat metabolism occur in which cycle :

a. Glycolysis b. Malate shuttle
c. Urea cycle d. Citric acid cycle

Q59. Methionine can enter the TCA cycle at which level:

a. fumarate b. Oxabacetate
c. Succinyl CoA d. Citrate

Q60. Anaplerotic reaction is catalyzed by:

a. Pyruvate carboxylase
b. Enolase
c. Pyruvate kinase
d. G6PD

Q61. In TCA cycle CO2 is released from:

a. Thiolase
b. Isocitrate dehydrogenase
c. Citrate dehydrogenase
d. alpha ketoglurate

Q62. Substrate level phosphorylation in TCA cycle involves:

a. Alpha keto glutarate dehydrogenase
b. Succinate thiokinase
c. Isocitrate dehydrogenase

46. a,c,e	47. c	48. b	49. c	50. c,d	51. c	52. b	53. a	54. b
55. a	56. b	57. a	58. d	59. c	60. a	61. b	62. b	

d. Fumarase
e. Malate dehydrogenase

Q63. TCA cycle does not take place in :

a. Hepatocyte b. Osteocyte
c. Neuron d. Erythrocyte

Q64. Proper functioning of krebs cycle doses not occur with deficiency of :

a. Thiamine b. Riboflavin
c. Vitamin E d. Vitamin K

Q65. What is the connecting link between urea cycle and TCA cycle

a. Fumarate b. Sucinate
c. Oxaloacetale d. Arginino sucinate

Q66. Normal renal threshold for glucose excretion is.....

a. 100 mg% b. 140 mg%
c. 180 mg% d. 80 mg%

Q67. Metabolite that is regarded as the dead end in glycolysis

a. Pyruvate
b. Lactate
c. 2, 3-bisphosphoglycerate
d. 3-phosphoglycerate

Q68. An example of an amphibolic pathway is

a. Glycolysis b. Beta oxidation
c. Citric acid cycle d. Alpha – oxidation

Q69. End product of the action of salivary amylase is:

a. Mannose b. Maltose
c. sucrose d. Fructose

Q70. Rate limiting step in gluconeogenesis:

a. Fructose 1, 6 bisphosphatase
b. Glucokinase
c. Fructokinase
d. None

Q71. GTP is a substrate for the following except

a. Pyruvate carboxykinase
b. Succinate thiokinase
c. Nucleoside diphosphate kinase
d. None of the above

Q72. Transketolase

a. Transfers two carbon fragments to an aldehyde acceptor
b. Transfers a three carbon Ketone containing fragments to an acceptor
c. Converts ribose5 phophate to xylulose 5phosphate
d. Concerts two five carbon sugar phosphates to fructose6phosphate and erythrose4phosphate

Q73. G6PD deficiency is-

a. Autosomal dominant
b. Autosomal recessive
c. X-linked dominant
d. X-linked recessive

Q74. Hexokinase is:

a. Ligase b. Transferase-
c. Oxidoreductase d. Reductase

Q75. Essential fructosuria is due to deficiency of

a. Beta-galactosidase
b. Aldolase-B
c. Fructokinase
d. Aldose reductase

Q76. Arsenite inhibits:

a. Enolase
b. G-6-PD
c. Phosphoglycerate Kinase
d. Hexokinase

Q77. Which of the following compounds inhibit phosphofructokinase?

a. ADP b. Citrate
c. AMP d. ATP

Q78. Regarding proteoglycans, false is:

a. Chondroitin sulfate is a proteoglycan
b. They hold less amount of water
c. They are made up of sugar and aminoacids
d. They carry charge

Q79. Glucose transporter in myocyte stimulated by insulin is

a. GLUT 1 b. GLUT 2
c. GLUT 3 d. GLUT 4

Q80. Hydrolysis of maltose will yield

a. Glucose only
b. Fructose + glucose
c. Galactose + glucose
d. Galactose + fructose

63. d	64. a,b	65. a	66. a	67. b	68. a	69. b	70. a	71. c
72. a	73. d	74. a	75. c	76. c	77. b,d	78. b	79. d	80. a

Q81. Which of the following is a component of polysaccharide?

a. Synovium b. Glucosamine
c. Glucoronic acid d. Ascorbic acid

Q82. Fructose is transported by

a. GLUT 5 b. GLUT 2
c. GLUT 3 d. GLUT 7

Q83. Which of the following is Aldosugar?

a. Fructose b. Erythrulose
c. Glucose d. None

Q84. The tissue with the highest glycogen content (mg/lOOmg)

a. Liver b. Muscle
c. Kidneys d. Testes

Q85. Chitin contains

a. Alfa 1-4 bond b. Alfa 1-6 bond
c. beta-1-6 bond d. beta-1-4 bond

Q86. Epimer combination(s) is/are

a. D-glucose & D-fructose
b. D-glucose & D-maltose
c. D-glucose & D-mannose
d. D-glucose & D-Aldose
e. D-galactose & D-glucose

Q87. Which of the following is the major proteoglycan of synovial fluid?

a. Chondroitin sulfate
b. Heparan sulfate
c. Dermatan sulfate
d. Hyaluronic acid

Q88. Mucopolysaccharidoses are caused by:

a. An increased rate of synthesis of proteoglycans
b. Defects in the degradation of proteoglycans
c. The synthesis of polysaccharides with an altered structure
d. An insufficient amount of proteolytic enzymes

Q89. Aggrecan are:

a. Meant for platelet aggregation
b. For adhesions of cells to basement membrane
c. For adhesion of fibrinogen receptors to plate
d. Proteoglycan found in cartilage

Q90. Anticoagulant used for preserving blood for prothrombin time estimation is :

a. Heparin b. Sodium citrate
c. Double oxalate d. Na

Q91. After overnight fasting levels of glucose transporters are reduced in :

a. Brain cells b. Heatocytes
c. Adipocytes d. RBCs

Q92. Regarding proteoglycans, false is :

a. Chondroitin sulfate is a proteoglycan
b. They hold less amount of water
c. They are made up of sugar and aminoacids
d. They carry charge

Q93. Reducing sugar in urine is seen in:

a. Fanconi anmia
b. Lactose intolerance
c. Galactosemia
d. Phenylketonuria
e. Salicylate poisoning

Q94. Following enzymes are involved in neoglucogenesis except:

a. Phosphoglycerate kinase
b. Fructose 1,6 biphosphatese
c. Phosphoglucomutase
d. Pyruvate carboxylase
e. Isomerase

Q95. Increased uric acid levels are seen in which glycogen storage disease?

a. Type I b. Type II
c. Type III d. Type IV

Q96. The molecule, which is the intiatior of cataract formation in the eye lens and whose 1 – phosphate derivative is responsible for liver failure is :

a. Sorbitol b. Mannitol
c. Inositol d. Galacticol

Q97. Fructose 2-6 biphosphate is:

a. Intermediate of glycosis
b. Positive allosteric regulation of PFK-1
c. Negative alloseric regulation of PFK-1
d. Positive allosteric regulation of PFK-2

81. b	82. a	83. c	84. a	85. d	86. d, c	87. d	88. b	89. d
90. b	91. c	92. b	93. c	94. c	95. a	96. d	97. b	

Q98. Essential Pentosuria is due to defect in:

a. HMP pathway
b. Glycolysis
c. Gluconeogenesis
d. Uronic acid pathway

Q99. Hemolytic anaemia is seen most commonly due to :

a. Pyruvate kinase
b. Phospho fructokinase I
c. Phosphoenolpyruvate carboxykinase
d. glucose 6- phosphatase

Q100. I-Cell disease is associated with:

a. Golgi apparatus
b. Lysosomes
c. Peroxisomes
d. Mitochondria

Q101. The activity of pyruvate carboxylase is dependent upon the positive allosteric effectors :

a. Succinate
b. AMP
c. Isocitrate
d. Acetyl CoA

Q102. Insulin like fractions are used as prebiotics as they are non digestible. Resistance to digestion in the upper GI tract results from:

a. Absence of digestive enzyme in the upper GIT
b. Beta configuration of of anomeic C2
c. Low pH of the stomach
d. Presence of α –Glycosidic linkages

Q103. Mechanism by which cytosolic pyruvate is transported to mitochondria is:

a. Chloride antiport
b. Proton symport
c. ATP dependent antiport
d. Facilitated uniport

Q104. Which of the following has no free aldehyde or ketone group

a. Fructose
b. Maltose
c. Sucrose
d. Galactose

Q105. Mc Ardles disease is due to the deficiency of –

a. Gluc-1, phosphatase
b. Gluc-1 , 6 diphosphatase
c. Myophosphorylase
d. hepatic phosphorylation

Q106. Which of the following symptoms is NOT seen in Von Gierke's disease?

a. Hepatomegaly
b. Hyperglycemia
c. Lactic aciodosis
d. Hyperlipidemia

Q107. Muscles are not involved in which glycogen storage disease

a. I
b. II
c. III
d. All of the above

Q108. Glycogen storage disease include all the following except

a. Von Gierke's disease
b. Fabry's disease
c. McArdle's disease McArdle's disease
d. Fragile syndrome
e. Krabbe's disease

Q109. Forbe's disease is due to deficiency of

a. Branching enzyme
b. Debranching enzyme
c. Myophosphorylase
d. Hepatic phosphorylase

Q110. Glucose 6 Phosphatase deficiency occurs in

a. Forbes disease
b. Niemann Pick disease
c. Von Gierke disease
d. Tay Sachs Disease

Q111. Pompe's disease is due to deficiency of which enzyme:

a. Branching enzyme
b. Glucose 6 phophatase
c. Acid maltase deficiency
d. Muscle phosphorylase

Q112. Glycogen storage diseases include

a. Niemann pick disease
b. McArdle's disease
c. Gaucher's disease
d. Pompe's disease
e. Tay Sachs disease

98. d	99. a	100. b	101. d	102. b	103. b	104. c	105. c
106. b	107. a	108. b, d, e,	109. b	110. c	111. c	112. b, d	

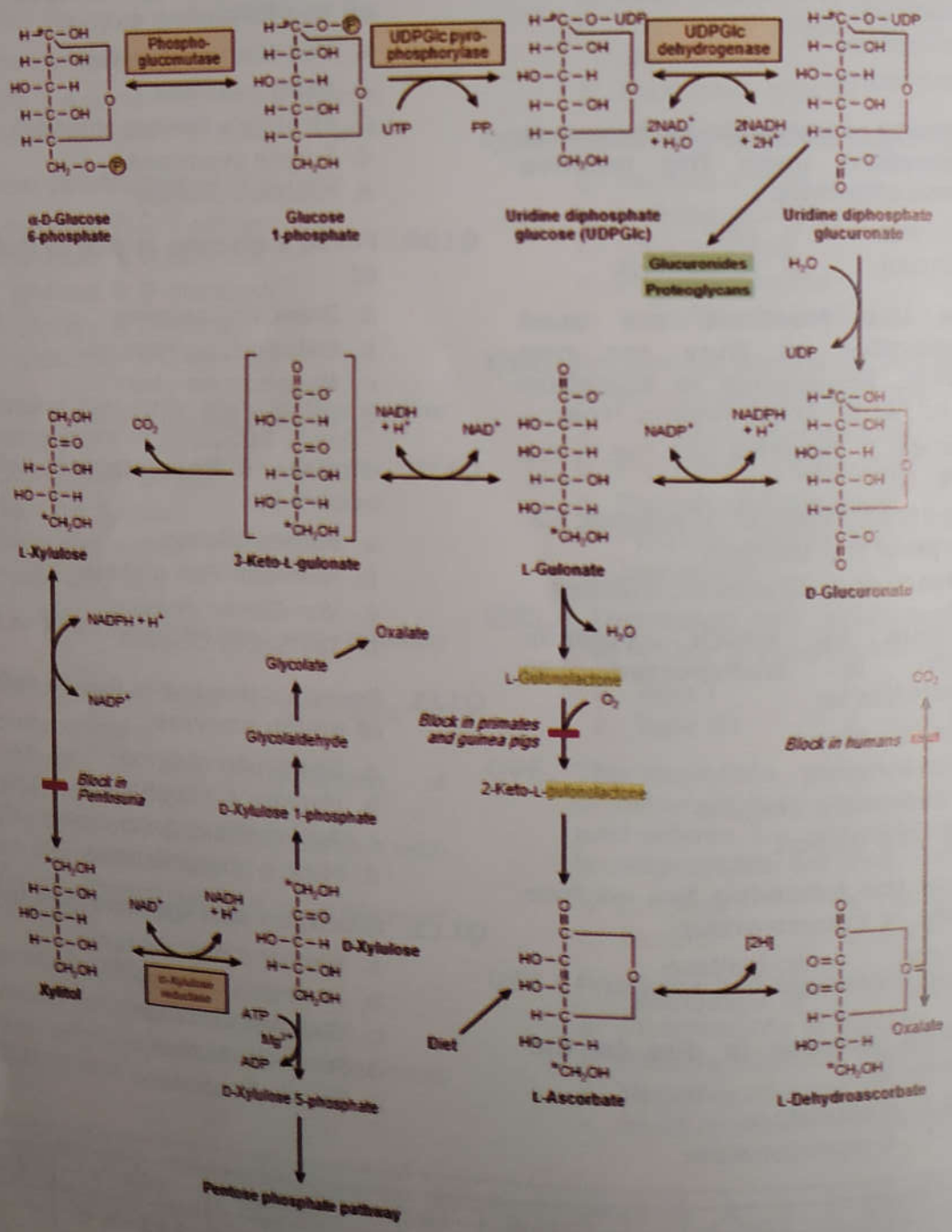
Carbohydrate Chemistry and Metabolism – Explanations

1. a) L-gulonolactone oxidase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. L-gulonolactone oxidase

In liver, the uronic acid pathway catalyzes the conversion of glucose to glucuronic acid, ascorbic acid (except in human beings and other species for which ascorbate is a vitamin, vitamin C), andpentoses. It is also an alternative oxidative pathway for glucose that, like the pentose phosphate pathway, does not lead to the formation of ATP. Glucuronate is reduced to l-gulonate, the direct precursor of ascorbate in those animals capable of synthesizing this vitamin, in an NADPH dependent reaction. In human beings and other primates, as well as guinea pigs, bats, and some birds and fishes, ascorbic acid cannot be synthesized because of the absence of L-gulonolactone oxidase.



b. Xylutitol reductase- In the rare benign hereditary condition essential pentosuria, considerable quantities of l-xylulose appear in the urine, because of absence of the enzyme necessary to reduce l-xylulose to xylitol.

c. Pyruvate dehydrogenase-link reaction between glycolysis and TCA Cycle.

d. UDP glucose dehydrogenase-it is involved in uronic acid pathway.

2. c) Accumulation of free radicals in RBC membrane

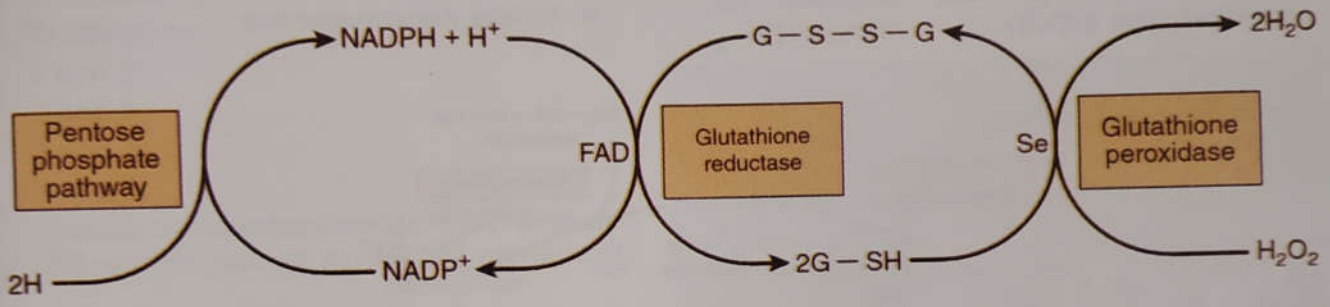
[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. 6-phosphogulonolactone not formed- In G6PD deficiency, 6-phosphogulonolactone is not formed. This is a true , But this is not cause of haemolysis.

b. Decreased oxidised glutathione –There is ↑ oxidised glutathione.

c. Accumulation of free radicals in RBC membrane –G6PD is a cytoplasmic enzyme catalysing the rate limiting step of HMP shunt.G6PD is the major source of NADPH

NADPH is the cofactor for glutathione reductase enzyme which maintains glutathione in the reduced state (G-SH).



Reduced glutathione is the major defence against oxidative damage of RBC membrane and protein. GGPD deficiency is an X-linked disorder predominantly affecting males. It gives protection against malaria. The person is asymptomatic unless he is exposed to oxidative stress like antimalarial drugs (primaquine), fava beans and severe infection. In deficiency of NADPH, glutathione can't be maintained in reduced state during oxidative stress. This leads to free radical mediated damage of RBC membrane and hemolysis.Free radical damage to homoglobin causes precipitation of Hb inside RECs as Inclusions known as Heinz bodies.

d. Due to methemoglobin formation –Methemoglobin reductase is NADPH dependant. But methamoglobin affects the oxygen carrying capacity of hemoglobin. It doesn't cause hemolysis.

3. a) Glucokinase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Glucokinase-

Case description is suggestive of Maturity Onset Diabetes of Young.

- MODY is due to mutation in single gene (monogenic).
- Subtypes of MODY are described according to the gene involved.
- Inherited in Autosomal dominant fashion
- Absence of autoantibodies
- Absence of ketosis

MODY2

- Glucokinase gene is located in chromosome 7.
- Glucokinase acts a sensor for glucose. It has high Km value. In β-cells of pancreas, It acts only when the glucose level is high and release the insulin.
- Due to mutation in Glucokinase, insulin is not released even when the glucose is high → Hyperglycemia.
- MODY2 is usually mild.

b. PFK –

No known relation with hyperglycemia.

c. Aldolase –

No known relation with hyperglycemia.

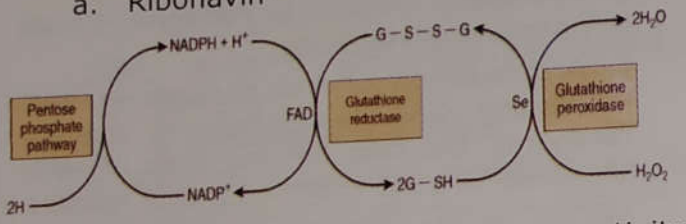
d. Enolase –

No known relation with hyperglycemia.

4. a) Riboflavin

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Riboflavin –



- Optimal glutathione reductase activity depends on adequate availability of Flavin adenine dinucleotide (FAD), a coenzyme derived from riboflavin(vitamin B-2).

b. Folicacid –is not required for transketolase activity.

c. VitaminC -is not required for transketolase activity.

d. VitaminE -is not required for transketolase activity.

5. c) 4

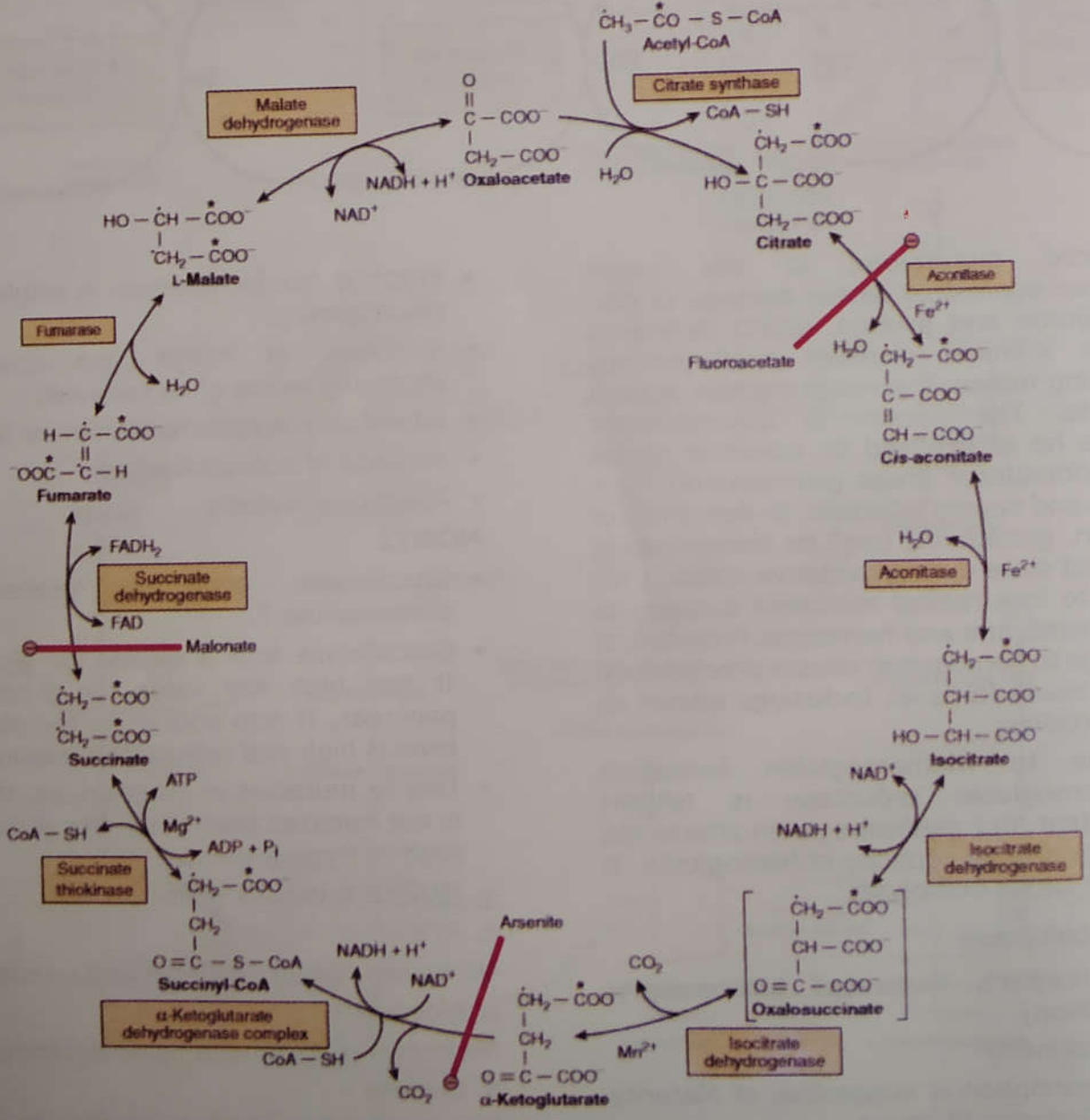
[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. 3

b. 2

c. 4 –

1. Isocitrate dehydrogenase
2. α-Ketoglutarate dehydrogenase complex
3. Succinate dehydrogenase
4. Malate dehydrogenase



d. 5

6. c) Glycogen

a. Glucose- yields 2 molecules of ATP under anaerobic metabolism

b. Galactose-is first converted to glucose and then can enter glycolysis to yield 3 molecules of ATP under anaerobic metabolism

c. Glycogen-forms Glucose 1 phosphate as it bypasses Glucokinase step and enters anaerobic metabolism to yields 3 ATP.

d. Amino acid-it is not carbohydrate to enter glycolysis.

7. d) 1 and 3

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Explanation:

1 and 2

3 and 4

2 and 3

1 and 3

Glucose transporters mediate the facilitated diffusion of glucose across the membrane.

Types of GLUT

Type	Organ distribution	Function
GLUT1	Brain, RBC, placenta, colon	Basal glucose uptake
GLUT2	Liver, pancreatic β cells, kidney	Glucose sensor* function
GLUT3	Brain, Kidney, placenta	Basal glucose uptake
GLUT4	Skeletal and cardiac muscle, adipose tissue	Insulin dependent uptake
GLUT5	Small intestine, SPERM	Fructose transporter*
GLUT6	Product of pseudogene	
GLUT7	Endoplasmic reticulum of hepatocytes	Glucose-6-phosphate transporter
GLUT12	Heart, skeletal muscle, brown adipose tissue, and prostate	Basal and insulin dependent uptake

EXTRA EDGE:

- Fanconi-Bickel disease is due to defect in GLUT2.

8. c) Succinate thiokinase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

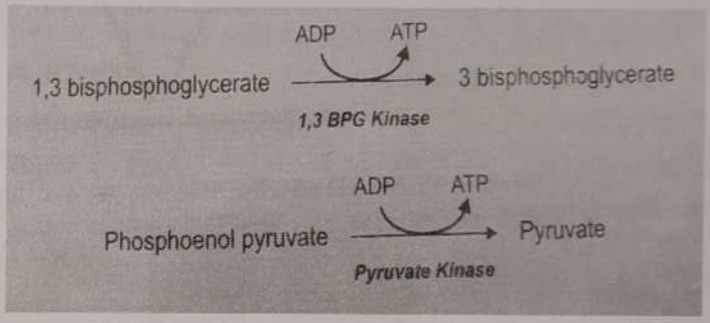
a. **Fumarase-**

Of TCA fumarase catalyzes the addition of water across the double bond of fumarate, yielding malate & is not involved in SLP.

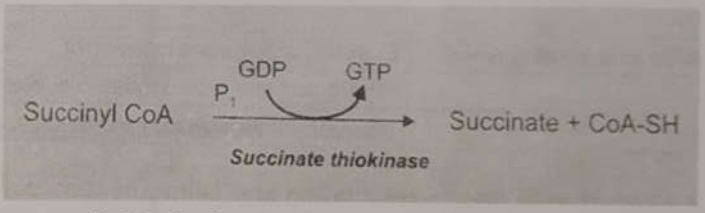
b. **Succinate dehydrogenase-** is not involved in SLP.

c. **Succinate thiokinase-**Succinyl-CoA is converted to succinate by the enzyme succinate thiokinase (succinyl-CoA synthetase). This is the only example in the citric acid cycle of substrate-level phosphorylation.

Glycolysis:



TCA Cycle:



d. Alpha ketoglutarate dehydrogenase- Ketoglutarate undergoes oxidative decarboxylation in a reaction catalyzed by a multi-enzyme complex similar to that involved in the oxidative decarboxylation of pyruvate, is not involved in SLP.

9. c) 6

Explanation:

Energy production of glucose from 2 molecules of lactate

Reaction	ATP required
Pyruvate carboxylase	2ATPs
Phosphoenol pyruvate carboxykinase	2GTPs/ATPs
Phosphoglycerate kinase	2ATPs
Total	6 ATPs

10. c) Presence of mitochondria

a. NADH

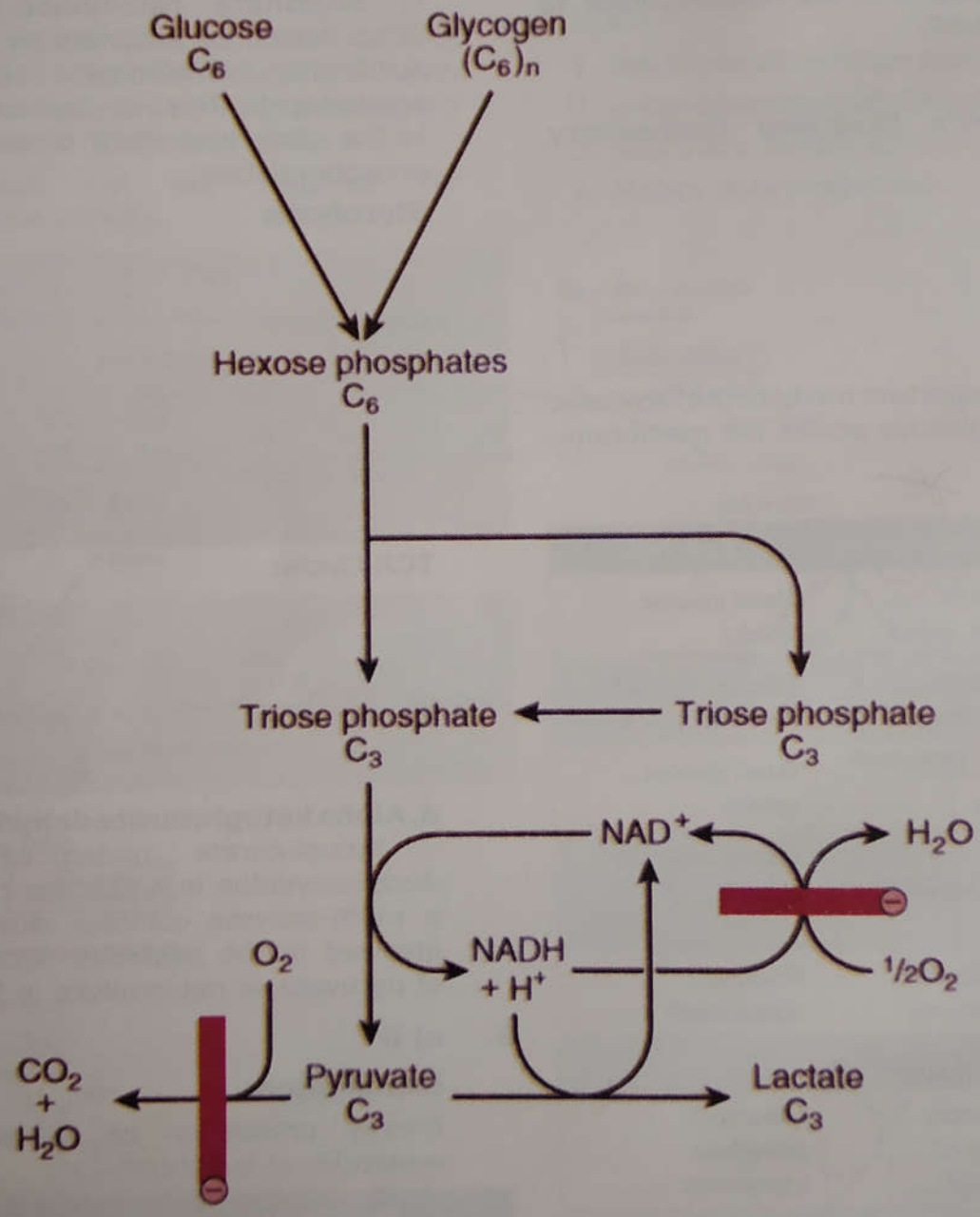
b. FADH2

c. Presence of mitochondria

RBC lacks mitochondria and utilize glucose through anaerobic glycolysis.

Glyceraldehyde 3 phosphate dehydrogenase reaction of glycolysis require NAD^+ as a cofactor.NADH can be converted to NAD^+ after donating the electrons to electron transport chain. If there is no mitochondria or there is no oxygen available, there is other way of regenerating the NAD^+.

If there is no mitochondria, to regenerate the NAD^+, pyruvate needs to be converted to lactate (anaerobic glycolysis).



d. Presence of low glucose

11. d) Phosphofructokinase I

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Regulatory and Adaptive Enzymes Associated with Carbohydrate Metabolism

	Activity in					
	Carbohydrate Feeding	Fasting and Diabetes	Inducer	Repressor	Activator	Inhibitor
Glycogenolsis, glycolysis, and pyruvate oxidation						
Glycogen synthase	↑	↓			Insulin, glucose-6-phosphate	Glucagon
Hexokinase						Glucose-6-phosphate
Glucokinase	↑	↓	Insulin	Glucagon		
P hosphofru ctokinase-1	↑	↓	Insulin	Glucagon	5'AMP, fructose - 6-phosphate, fructose 2, 6-bisphosphate, P_i	Citrate, ATP, glucagon
Pyruvate kinase	↑	↓	Insulin, fructose	Glucagon	Fructose 1,6-bisphosphate, insulin	ATP, alanine, glucagon, norepinephrine
Pyruvate dehydrogena se	↑	↓			CoA, NAD^+, insulin, ADP, pyruvate	Acetyl CoA, NADH, ATP [fatty acids, ketone bodies)
Gluconeogenesis						
Pyruvate carboxylase	↓	↑	Glucocorticoids, glucagon, epinephrine	Insulin	Acetyl CoA	ADP
Phosphoenol pyruvate carboxykinase	↓	↑	Glucocorticoids, glucagon, epinephrine	Insulin	Glucagon	
Glucose 6-phosphatase	↓	↑	Glucocorticoids, glucagon, epinephrine	Insulin		

12. d) Phosphorylase enzyme

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Muscle debranching enzyme-Limit dextrins would be seen in muscle biopsy instead of intact glycogen.

b. Phosphofructokinase I- lead to haemolytic anaemia.

c. Glucose-6 phosphatase- lead to Von Gierke disease

d. Phosphorylase enzyme-It is Mc Ardle disease. Deficiency of muscle glycogen phosphorylase enzyme. So the first step of glycogen breakdown will not occur. Thus intact glycogen is seen in muscle biopsy.

13. a) TCA cycle

[Ref: Harper's Illustrated biochemistry, 30th Edition]

The poison fluoroacetate is found in some of plants, and their consumption can be fatal to grazing animals. Some fluorinated compounds used as anticancer agents and industrial chemicals (including pesticides) are metabolized to fluroacetate. It is toxic because fluoroacetyl-COA condenses with oxaloacetate to form fluorocitrate, which inhibits aconitase, causing citrate to accumulate.Other inhibitors of citric acid cycle-Malonate, Arsenite.

Enolase requires Mg^{++}, and by removing magnesium ions, fluoride will irreversibly inhibit this enzyme. Thus, fluoride will stop the whole glycolysis. So when taking blood for sugar estimation, fluoride is added to blood or taking the sample into tubes containing fluoride. If not, glucose is metabolized by the blood cells, so that lower blood glucose values are obtained.

14. b) Adipose tissue

[Ref: Harper's illustrated biochemistry, 30th Edition]

	Tissue Location	Functions
Facilitative bidirectional transporters		
GLUT 1	Brain, kidney, colon, placenta, erythrocytes	Glucose uptake
GLUT 2	Liver, pancreatic β cell, small intestine, kidney	Rapid uptake or release of glucose
GLUT 3	Brain, kidney, placenta	Glucose uptake
GLUT 4	Heart and skeletal muscle, adipose tissue	Insulin-stimulated glucose uptake
GLUTS	Small intestine	Absorption of fructose
Sodium-dependent unidirectional transporter		
SGLT1	Small intestine and kidney	Active uptake of glucose against a concentration gradient

15. b) Keratin sulfate

[Ref: Lippincott's illustrated reviews, 6th Edition]

Glycosaminoglycans	Composition	Key features
Chondroitin sulfate	Glucuronic acid + N- acetyl galactosamine sulfate	Most abundant GAG in the body
Dermatan sulfate	Iduronic acid + N- acetyl galactosamine	
Keratin sulfate	Galactose + N- acetyl glucosamine	No acidic sugars
Heparin sulfate	Same as heparin (minimal acetylation)	
Heparin	Glucuronic acid + glucosamine	Only intracellular GAG in the body and most powerful anticoagulant
Hyaluronic acid	Glucuronic acid + N- acetyl glucosamine	Only GAG not limited to animals. Found in bacteria

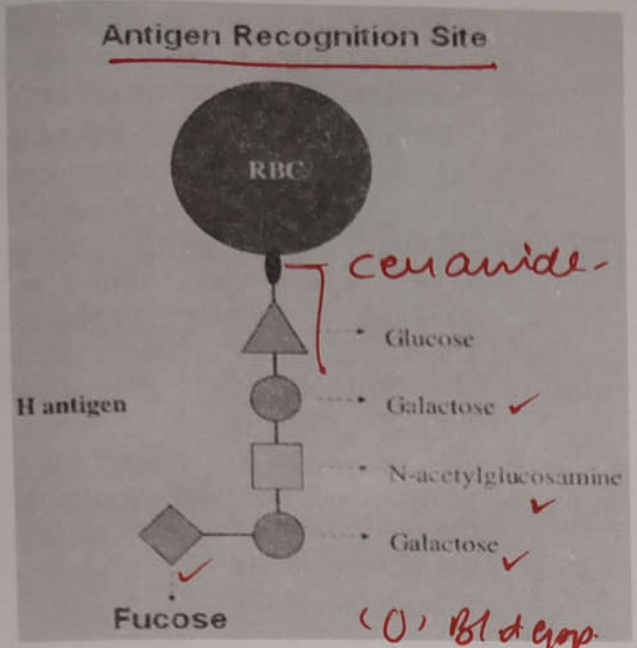
16. a) Fucose

[Ref: Harper's Illustrated Biochemistry, 29th edition]

Explanation:

Antigen recognizing site in RBCs

- The different blood types in the ABO system arise from the existence of similar molecules on the RBC membrane
- In each type (A, B or O), the "base unit" is the same
- A protein with a lipid known as ceramide is associated
- Four sugars extend from the ceramide into the extracellular fluid
- These sugars (in order from the ceramide) are galactose- N-acetyl-galactosamine – galactose.
- The last galactose also has a fucose at right angles to it.
- This base unit is referred to as the "H-antigen" and is the unit present on Type O blood.
- Type A and Type B blood are distinguished by the addition of a fifth sugar
- Type A blood has an additional N-acetylgalactosamine on the end
- Type B blood has a galactose as the fifth sugar.



17. **a) Hexokinase**
b) Pyruvate kinase
c) Phosphofructokinase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Glycolysis is Regulated at three Steps involving

- hexokinase (and glucokinase)
- phosphofructokinase
- pyruvate kinase

18. **c)** Sucrose
e) Trehalose

[Ref: Lippincott's illustrated reviews, 6th Edition]

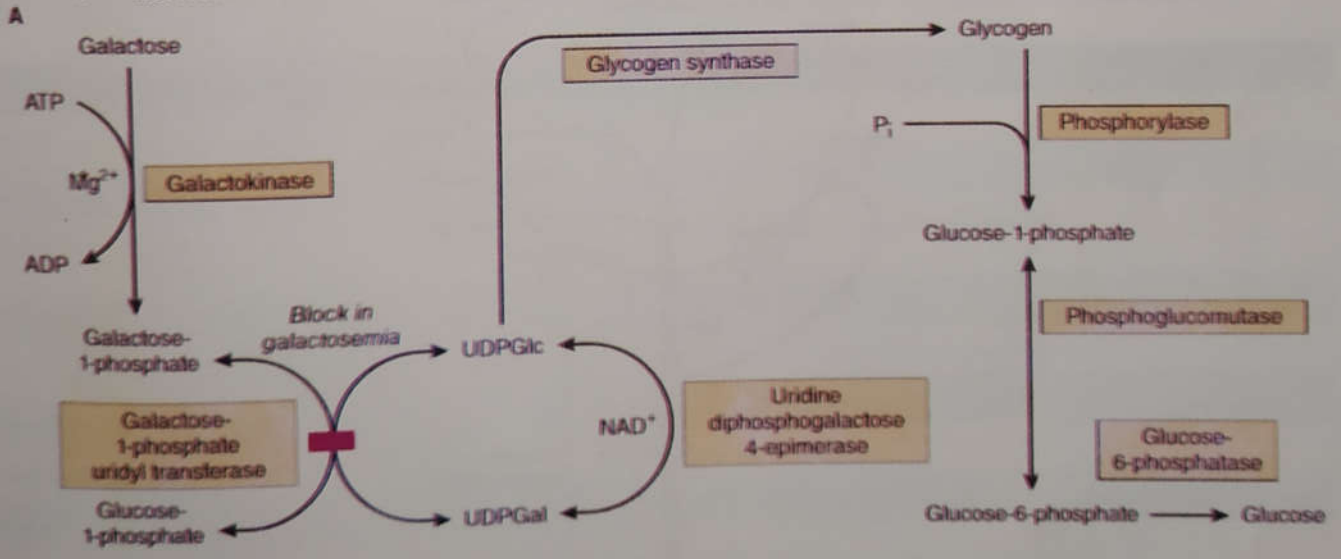
Reducing Sugars:

- The sugar can act as a reducing agent, and is termed a reducing sugar. Such sugars can react with chromogenic agents (for example, Benedict's reagent or Fehling's solution) causing the reagent to be reduced and colored, with the aldehyde group of the acyclic sugar becoming oxidized. (Note: Only the state of the oxygen in the aldehyde group determines if the sugar is reducing or non-reducing]
- Reducing substance: Reducing sugars (glucose, fructose, galactose, xylulose, lactose), amino acids, ascorbic acid. and certain drugs: and drug metabolites.
- Sucrose is not a reducing sugar

19. **All**

[Ref: Harper 30th Edition & Lippincott 6th Edition]

a. **Galactose synthesis-involves UDP glucose**



b. **Glycogen synthesis-** UDPG can donate glucose to a "Primer" molecule of glycogen and is involved in glycogen synthesis.

c. **Bilirubin metabolism-**UDP-Glucuronic Acid is used for Conjugation and detoxication of bilirubin, benzoic acid, sterols, estrogens and drugs

d. **Ganglioside synthesis-** serves as a precursor of sucrose lipopolysaccharides, and glycosphingolipids.

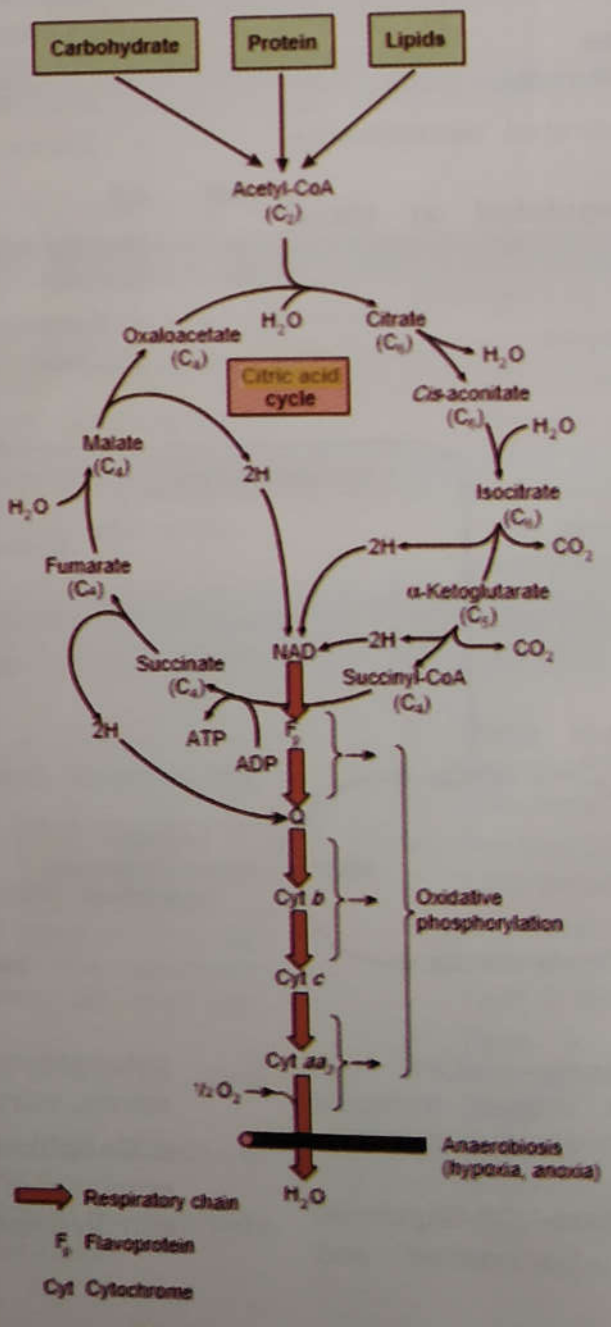
Heparin synthesis-Also used in the biosynthesis of hyaluronic acid, heparin, and several other MPS.

20. b) Alpha keto-glutarate is a five carbon molecule

[Ref: Harper's Illustrated biochemistry, 30th Edition]

The Krebs or Tricarboxylic Acid Cycle

- The citric acid cycle is a sequence of reactions in mitochondria that oxidizes the acetyl moiety of acetyl-CoA to CO_2 and reduces coenzymes that are reoxidized through the electron transport chain, linked to the formation of ATP.
- The cycle starts with reaction between the acetyl moiety of acetyl-CoA and the four-carbon dicarboxylic acid oxaloacetate, forming a six-carbon tricarboxylic acid, citrate.
- The citric acid cycle provides the main pathway for ATP formation linked to the oxidation of metabolic fuels.
- During the oxidation of acetyl-CoA, coenzymes are reduced and subsequently reoxidized in the respiratory chain, liked to the formation of ATP (oxidative phosphorylation).
- This process is aerobic requiring oxygen as the final oxidant of the reduced coenzymes. The enzymes of the citric acid cycle are located in the mitochondrial matrix.



21. b) G6PD

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. **LDH:**

Lactate dehydrogenase is comprised of two domains, an N-terminal NAD+-binding domain and a C-terminal binding domain for the second substrate, pyruvate. Lactate dehydrogenase is one of the family of oxidoreductase that share a common N-terminal NAD(P)+-binding domain known as the Rossmann fold.

b. **G6PD:**

Dehydrogenation of glucose-6-phosphate to 6-phosphogluconate occurs via the formation of 6-phosphogluconolactone, catalyzed by glucose 6-phosphate dehydrogenase, an NADP dependent enzyme. The hydrolysis of 6-phospho gluconolactone is accomplished by the enzyme gluconolactone hydrolase. A second oxidative step is catalyzed by 6-phosphogluconate dehydrogenase, which also requires NADP+ as hydrogen acceptor. Decarboxylation follows with the formation of the ketopentose ribulose-5-phosphate.

c. **G3PD:**

By fusing a segment of DNA coding for a Rossmann fold domain to that coding for a variety of C-terminal domains, a large family of oxidoreductases have evolved that utilize NAD(P)+/NAD(P)H for the oxidation and reduction of a wide range of metabolites. Examples include alcohol dehydrogenase, glyceraldehyde-3-phosphate dehydrogenase, malate dehydrogenase, quinone oxidoreductase, 6-phosphogluconate dehydrogenase, d-glycerate dehydrogenase, formate dehydrogenase, and 3α, 20β-hydroxysteroid dehydrogenase.

d. **Alcohol dehydrogenase:**

By fusing a segment of DNA coding for a Rossmann fold domain to that coding for a variety of C-terminal domains, a large family of oxidoreductases have evolved that utilize NAD(P)+/NAD(P)H for the oxidation and reduction of a wide range of metabolites. Examples include alcohol dehydrogenase.

22. d) 4

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. 1- insulin independent transporter

b. 2 -insulin independent transporter

c. 3- insulin independent transporter

d. 4- insulin dependent transporter

	Tissue Location	Functions
Facilitative bidirectional transporters		
GLUT 1	Brain, kidney, colon, placenta, erythrocytes	Glucose uptake
GLUT 2	Liver, pancreatic β cell, small intestine, kidney	Rapid uptake or release of glucose
GLUT 3	Brain, kidney, placenta	Glucose uptake
GLUT 4	Heart and skeletal muscle, adipose tissue	Insulin-stimulated glucose uptake
GLUTS	Small intestine	Absorption of fructose
Sodium-dependent unidirectional transporter		
SGLT1	Small intestine and kidney	Active uptake of glucose against a concentration gradient

23. c) Brain

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. RBCs- Erythrocytes lack mitochondria and hence are wholly reliant on (anaerobic) glycolysis.

b. Lens-anaerobic glycolysis occurs in lens.

c. Brain-aerobic glycolysis.

d. Testis- anaerobic glycolysis occurs in lens.

24. b) Glucose-6-Phosphate

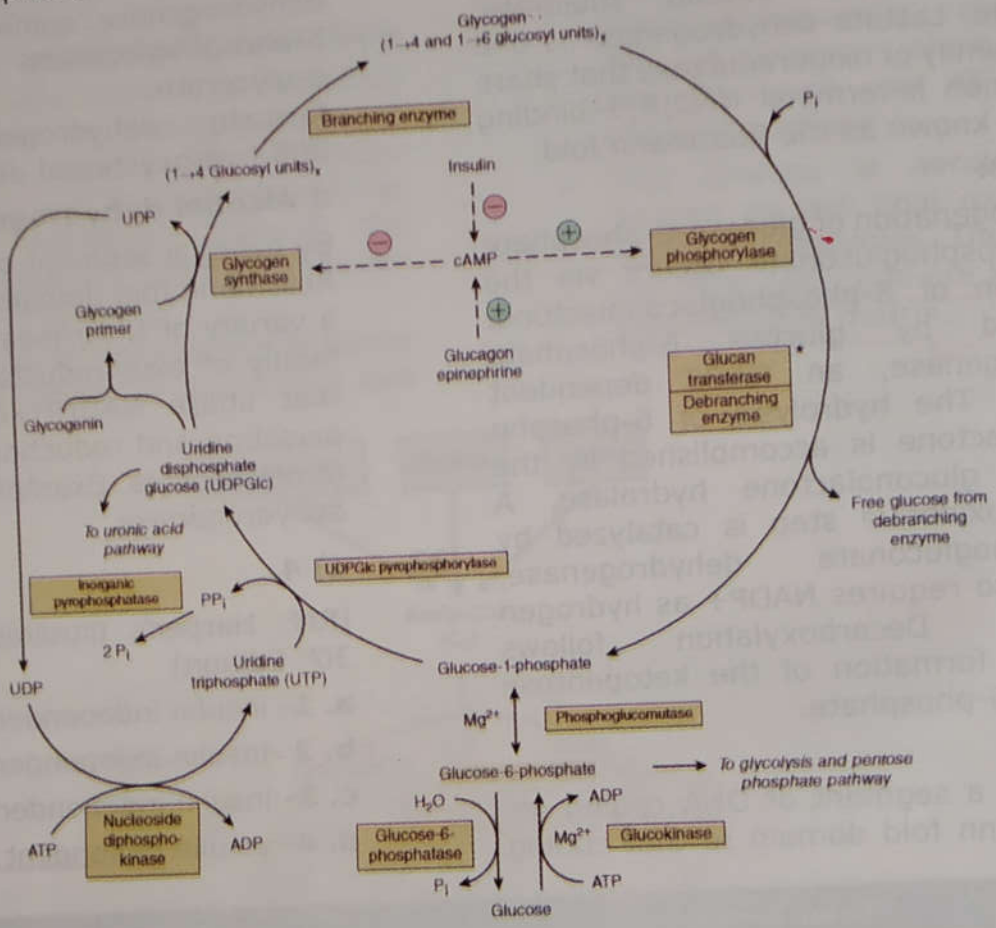
[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Galactose-1-phosphate-is not present in any of these pathways.

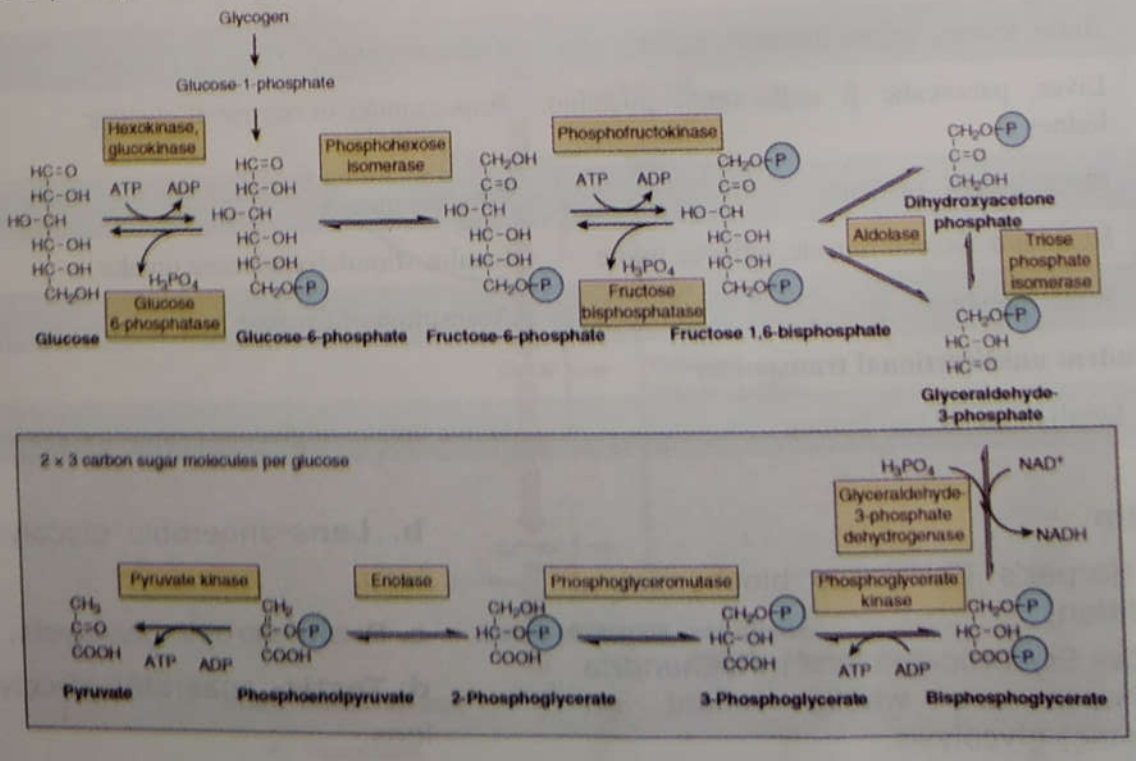
b. Glucose-6-Phosphate-

Glucose 6-phosphate is an important compound at the junction of several metabolic pathways: glycolysis, gluconeogenesis,the pentose phosphate pathway , glycogenesis, and glycogenolysis.

Glucose-6-Phosphate in glycogenesis and glycogenolysis.



Glucose 6 phosphate in glycolysis:



Glucose 6 phosphate is also seen in gluconeogenesis as it is reversal of glycolysis.

c. Uridinediphosphoglucose - is involved in

- uronic acid pathway
- galactose metabolism
- Interrelationships in metabolism of amino sugars.
- Glycosphingolipids synthesis- Biosynthesis of gangliosides.

d. Fructose-6-phosphate- is involved in

- Glycolysis
- Gluconeogenesis
- Fructose metabolism

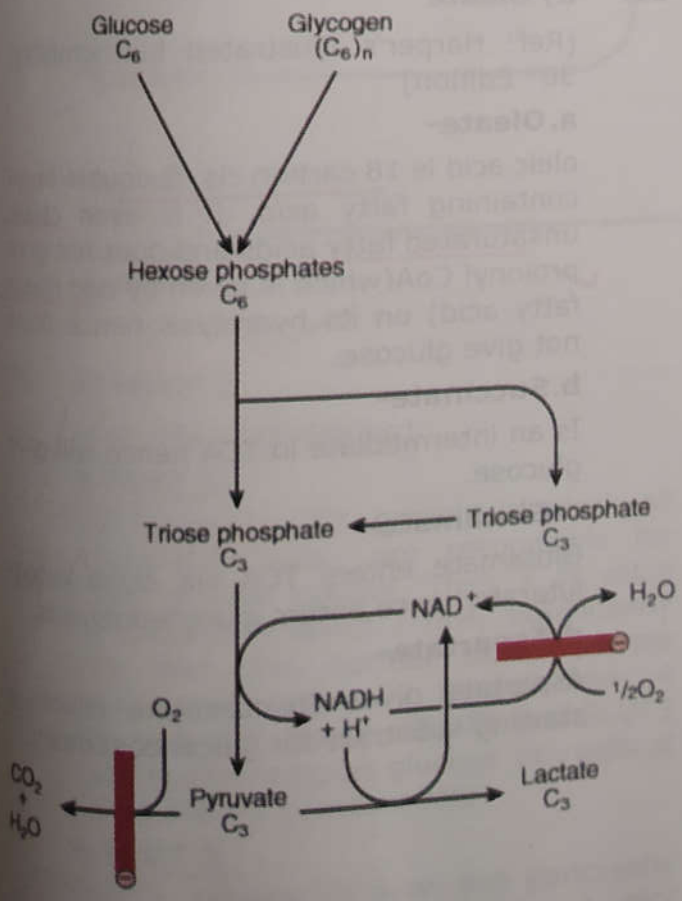
25. c) Lactate

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Pyruvate -is end product in aerobic glycolysis

b. Acetyl CoA-is formed in link reaction between glycolysis and TCA Cycle.

c. Lactate -



Summary of glycolysis. ⊖, blocked under anaerobic conditions or by absence of mitochondria containing key respiratory enzymes, as in erythrocytes.

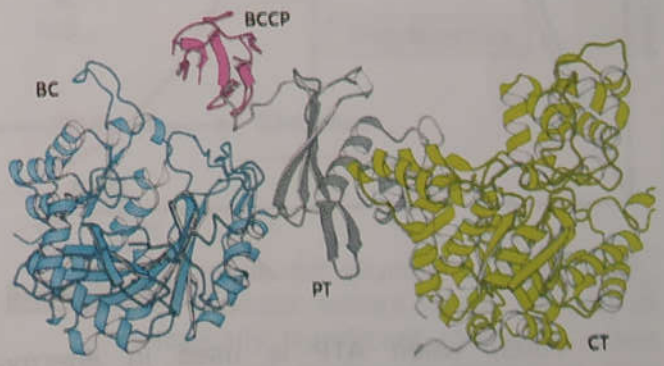
d. Oxaloacetate-is substrate for gluconeogenesis.

26. a) Biotin is required

[Ref: Stryer 8th Edition]

a. Biotin is required-

Pyruvate carboxylase functions as a tetramer composed of four identical subunits, and each subunit consists of four domains. The biotin carboxylase domain (BC) catalyzes the formation of carboxyphosphate and the subsequent attachment of CO 2 to the second domain, the biotin carboxyl carrier protein (BCCP), the site of the covalently attached biotin. Once bound to CO 2, BCCP leaves the biotin carboxylase active site and swings almost the entire length of the subunit (<75Å) to the active site of the pyruvate carboxylase domain (PC), which transfers the CO 2 to pyruvate to form oxaloacetate. BCCP in one subunit interacts with the active sites on an adjacent subunit. The fourth domain (PT) facilitates the formation of the tetramer.



A subunit of pyruvate carboxylase. Biotin, covalently attached to the BCCP, transports CO2 from the BC active site to the PC active site of an adjacent subunit. (BC) biotin carboxylase; (BCCP) biotin carboxyl carrier protein; (PC) pyruvate carboxylase; (PT) pyruvate carboxylase tetramerization domain.

b. Glucagon is an inhibitor-glucagon promotes gluconeogenesis

c. Lactate is essential intermediate- lactate can be a starting substrate for gluconeogenesis but is essentially not an intermediate.

d. Occurs in cytoplasm - gluconeogenesis occurs both in cytosol and mitochondria.

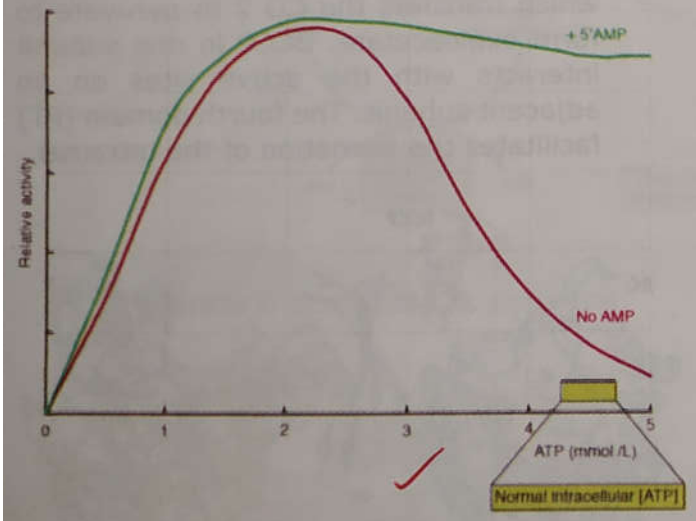
27. b) Citrate

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. AMP-

Phosphofructokinase (phosphofructokinase-1) occupies a key position in regulating glycolysis and is also subject to feedback control. It is activated by 5′ AMP. At the normal intracellular [ATP] the enzyme is about 90% inhibited; this inhibition is reversed by 5′AMP. 5′ AMP acts as an indicator of the energy status of the cell. The presence of adenylyl kinase in liver and many other tissues allows rapid equilibration of the reaction

$2ADP \leftrightarrow ATP + 5' AMP$.



Thus, when ATP is used in energy-requiring processes, resulting in formation of ADP, [AMP] increases. A relatively small decrease in [ATP] causes a several-fold increase in [AMP], so that [AMP] acts as a metabolic amplifier of a small change in [ATP], and hence a sensitive signal of the energy state of the cell. The activity of phosphofructokinase-1 is thus regulated in response to the energy status of the cell to control the quantity of carbohydrate undergoing glycolysis prior to its entry into the citric acid cycle. At the same time, AMP activates glycogen phosphorylase, so increasing glycogenolysis.

b. Citrate-

Phosphofructokinase (phosphofructokinase-1) occupies a key position in regulating glycolysis and is also subject to feedback control. It is inhibited by citrate and by normal intracellular concentrations of ATP and is activated by 5′ AMP.

c. Glucose 6 phosphate-

A consequence of the inhibition of phosphofructokinase-1 by ATP is an accumulation of glucose-6-phosphate, which in turn inhibits further uptake of glucose in extrahepatic tissues by inhibition of hexokinase.

d. Insulin-

Insulin favors glycolysis and inhibits gluconeogenesis.

28. a) Oleate

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Oleate-

oleic acid is 18 carbon cis -9 double bond containing fatty acid. It is even chain unsaturated fatty acids and does not give proionyl CoA(which is given by odd chain fatty acid) on its hydrolysis hence does not give glucose.

b. Succinate-

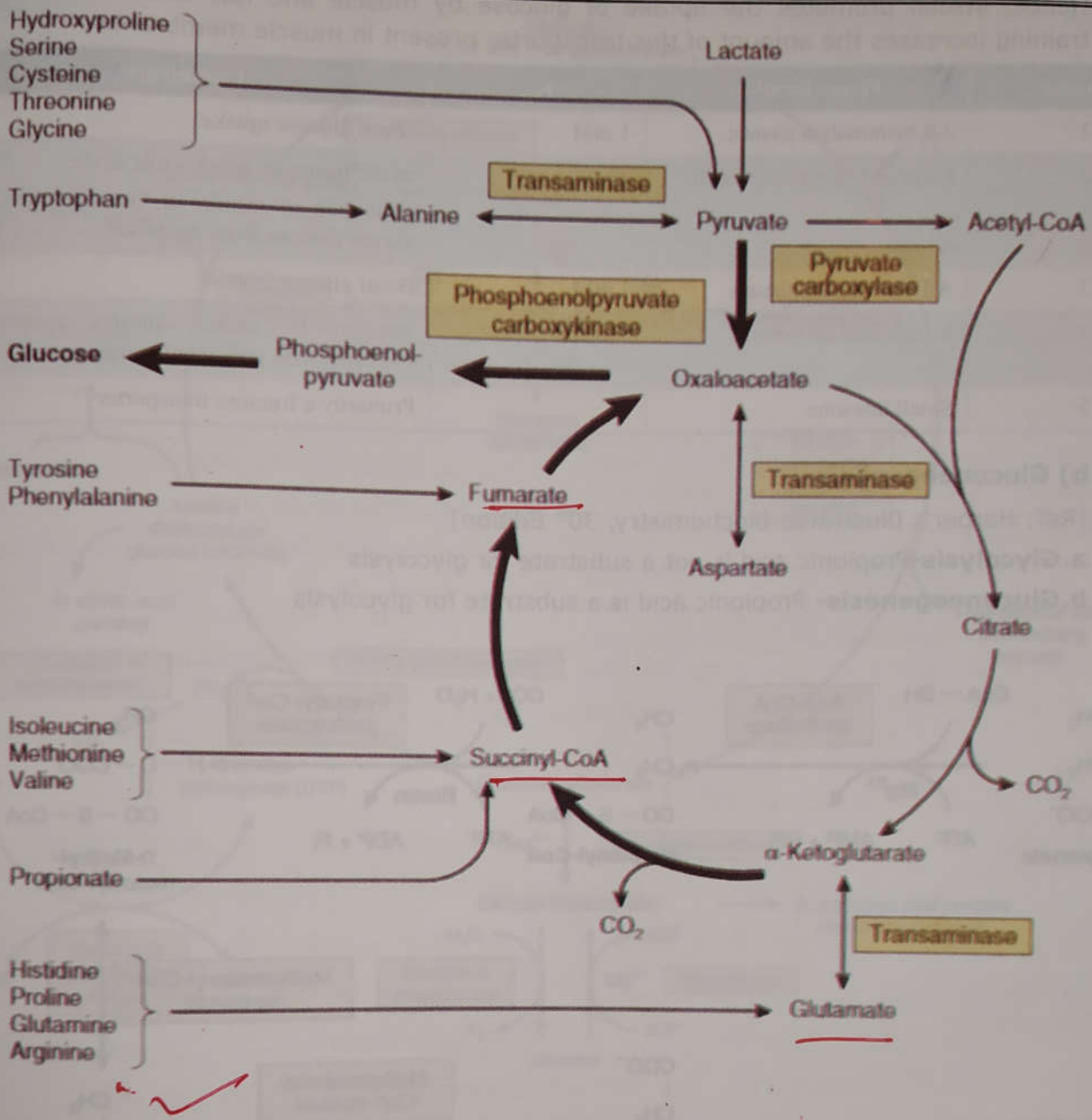
Is an intermediate in TCA hence will give glucose.

c. Glutamate-

Glutamate enters TCA via alpha-ketoglutarate hence enters gluconeogenesis.

d. Aspartate-

Aspartate gives Oxaloacetate which is starting substrate for gluconeogenesis.



29. b) GLUT 2

[Ref: Stryer 8th Edition]

a. GLUT 1-

GLUT1 and GLUT3, present in nearly all mammalian cells, are responsible for basal glucose uptake. Their K M value for glucose is about 1 mM, significantly less than the normal serum-glucose level, which typically ranges from 4 mM to 8 mM. Hence, GLUT1 and GLUT3 continually transport glucose into cells at an essentially constant rate.

b. GLUT 2-

GLUT2, present in liver and pancreatic b cells, is distinctive in having a very high K_M value for glucose (15–20 mM). Hence, glucose enters these tissues at a biologically significant rate only when there is much glucose in the blood. The pancreas can sense the glucose level and accordingly adjust the rate of insulin secretion. The high K_M value of GLUT2 also ensures that glucose rapidly enters liver cells only in times of plenty.

c. GLUT 3 -SEE EXPL.OF A

d. GLUT 4- GLUT4, which has a K_M value of 5 mM, transports glucose into muscle and fat cells. The number of GLUT4 transporters in the plasma membrane increases rapidly in the presence of insulin, which signals the fed state.

Hence, insulin promotes the uptake of glucose by muscle and fat. Endurance exercise training increases the amount of this transporter present in muscle membranes.

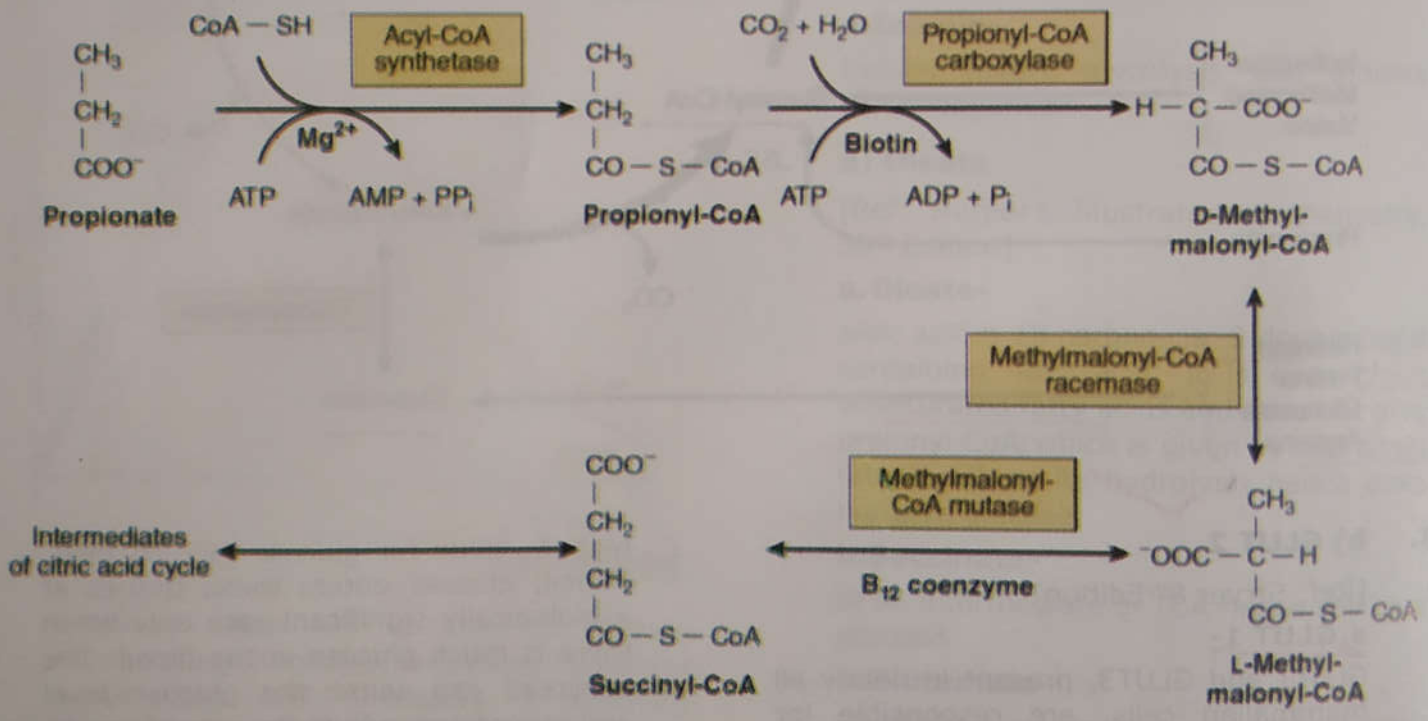
Name	Tissue location	K_M	Comments
GLUT1	All mammalian tissues	1 mM	Basal glucose uptake
GLUT2	Liver and pancreatic p cells	15-20 mM	In the pancreas, plays a role in the regulation of insulin In the liver, removes excess glucose from the blood
GLUT3	All mammalian tissues	1 mM	Basal glucose uptake
GLUT4	Muscle and fat cells	5 mM	Amount In muscle plasma membrane increases with endurance training
GLUT5	Small intestine	-	Primarily a fructose transporter

30. b) Gluconeogenesis

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Glycolysis-Propionic acid is not a substrate for glycolysis

b. Gluconeogenesis- Propionic acid is a substrate for glycolysis



c. Glycogenolysis- Propionic acid is not a substrate for glycolysis

d. None

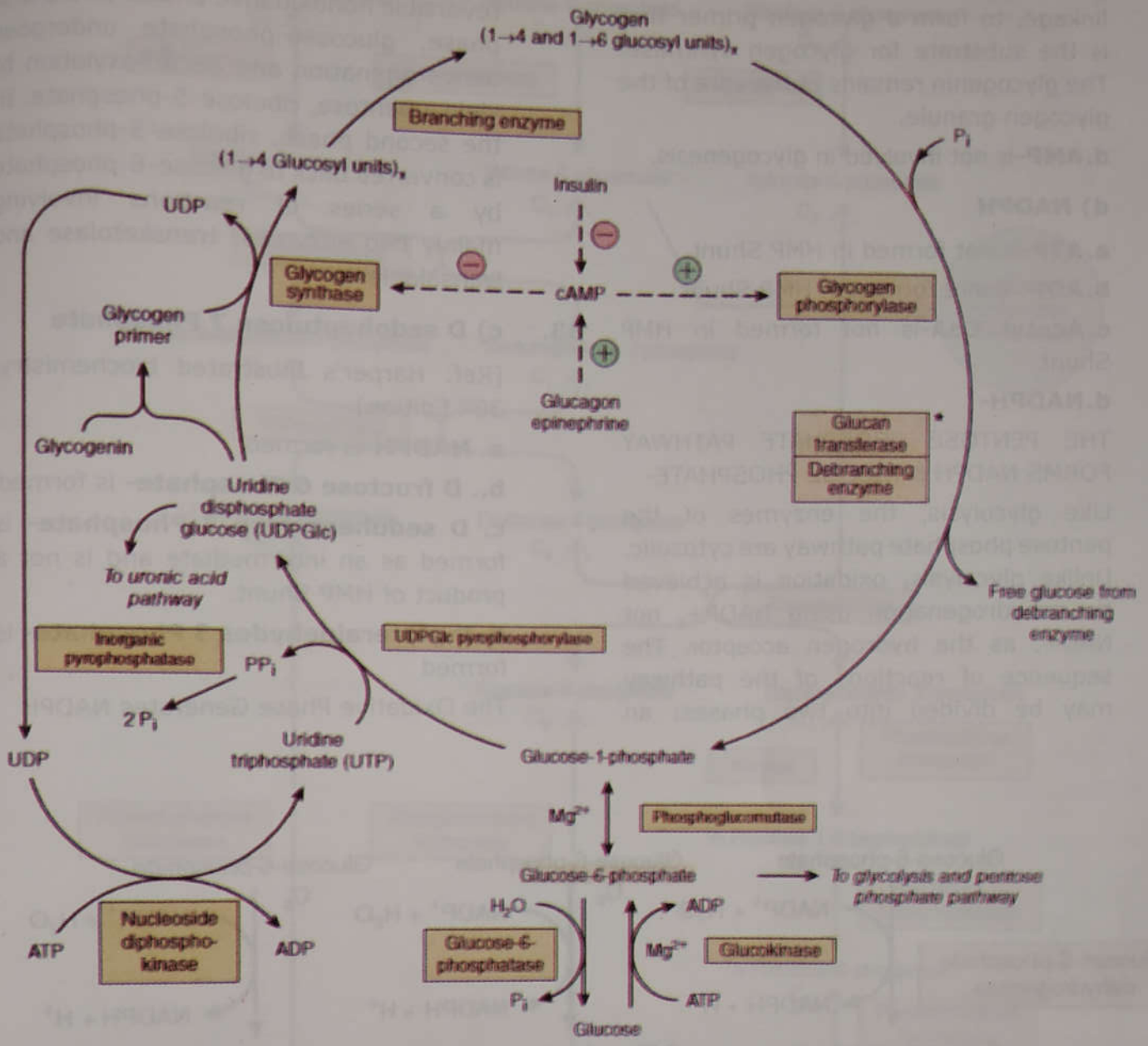
31. c) UTP

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. GTP-is not involved in glycogenesis.

b. GDP-is not involved in glycogenesis.

c. UTP-is involved in glycogenesis.



Glucose-6-phosphate is isomerized to glucose-1-phosphate by phosphoglucomutase. The enzyme itself is phosphorylated, and the phosphate group takes part in a reversible reaction in which glucose 1,6-bisphosphate is an intermediate. Next, glucose-1-phosphate reacts with uridine triphosphate (UTP) to form the active nucleotide uridine diphosphate glucose (UDPGlc) and pyrophosphate, catalyzed by UDPGlc pyrophosphorylase. The reaction proceeds in the direction of UDPGlc formation because pyrophosphatase catalyzes hydrolysis of pyrophosphate to 2 × phosphate, so removing one of the reaction products. UDPGlc pyrophosphorylase has a low Km for glucose-1-phosphate and is present in relatively large amounts, so that it is not a regulatory step in glycogen synthesis.

The initial steps in glycogen synthesis involve the protein glycogenin, a 37-kDa protein that is glucosylated on a specific tyrosine residue by UDPGlc. Glycogenin catalyzes the transfer of a further seven

glucose residues from UDPGlc, in 1 → 4 linkage, to form a glycogen primer that is the substrate for glycogen synthase. The glycogenin remains at the core of the glycogen granule.

d. AMP-is not involved in glycogenesis.

32. d) NADPH

a. ATP-is not formed in HMP Shunt

b. ADP -is not formed in HMP Shunt

c. Acetyl CoA-is not formed in HMP Shunt

d. NADPH-

THE PENTOSE PHOSPHATE PATHWAY FORMS NADPH & RIBOSE PHOSPHATE-

Like glycolysis, the enzymes of the pentose phosphate pathway are cytosolic. Unlike glycolysis, oxidation is achieved by dehydrogenation using NADP+, not NAD+, as the hydrogen acceptor. The sequence of reactions of the pathway may be divided into two phases: an irreversible oxidative phase and a reversible nonoxidative phase. In the first phase, glucose6-phosphate undergoes dehydrogenation and decarboxylation to yield a pentose, ribulose-5-phosphate. In the second phase, ribulose-5-phosphate is converted back to glucose-6-phosphate by a series of reactions involving mainly two enzymes: transketolase and transaldolase.

33. c) D sedoheptulose 7 Phosphate

[Ref: Harper's Illustrated biochemistry, 30th Edition]

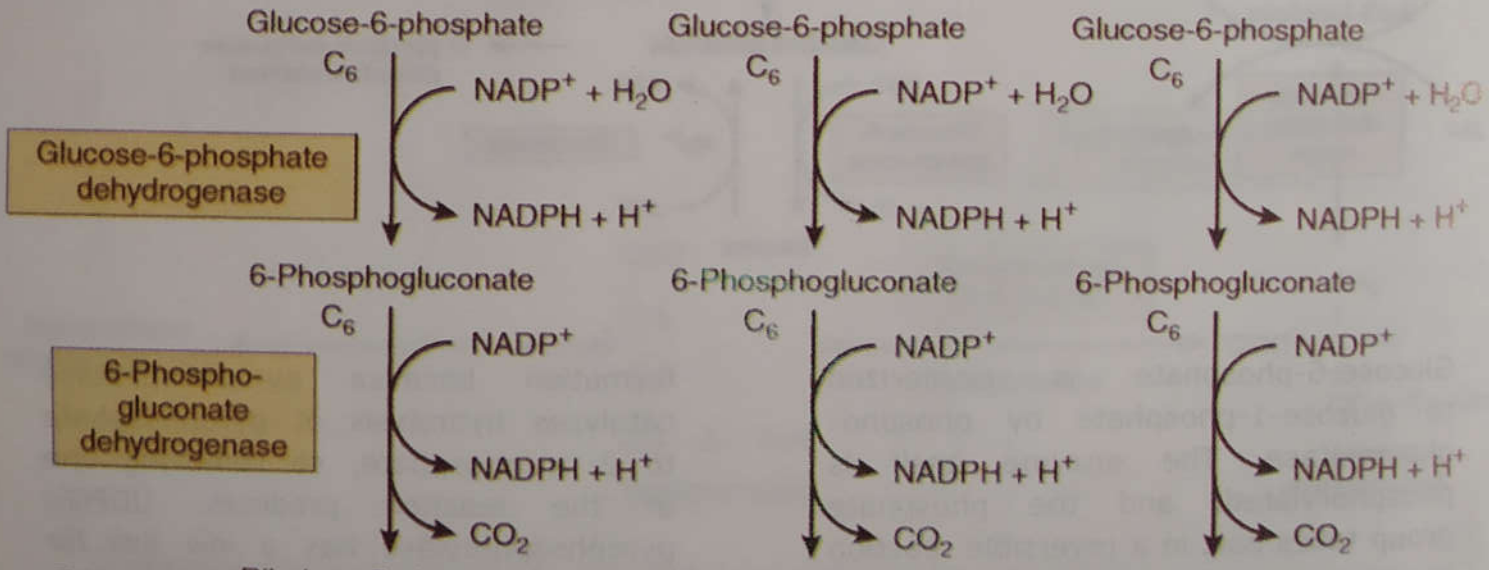
a. NADPH-is formed

b.. D fructose 6 Phosphate- is formed

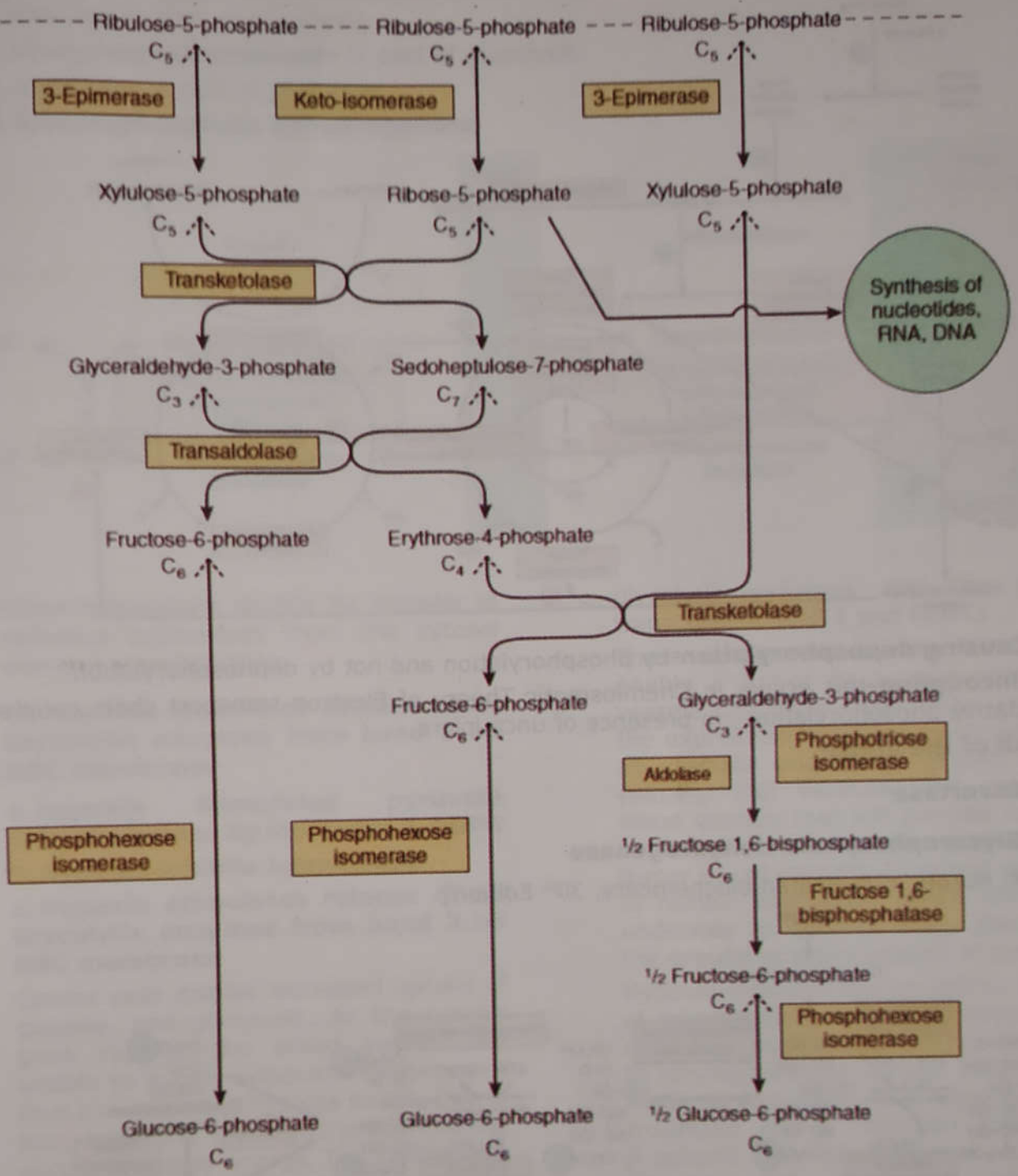
c. D sedoheptulose 7 Phosphate- is formed as an intermediate and is not a product of HMP Shunt.

d. D glyceraldehydes 3 Phosphate- is formed

The Oxidative Phase Generates NADPH



The Nonoxidative Phase Generates Ribose Precursors



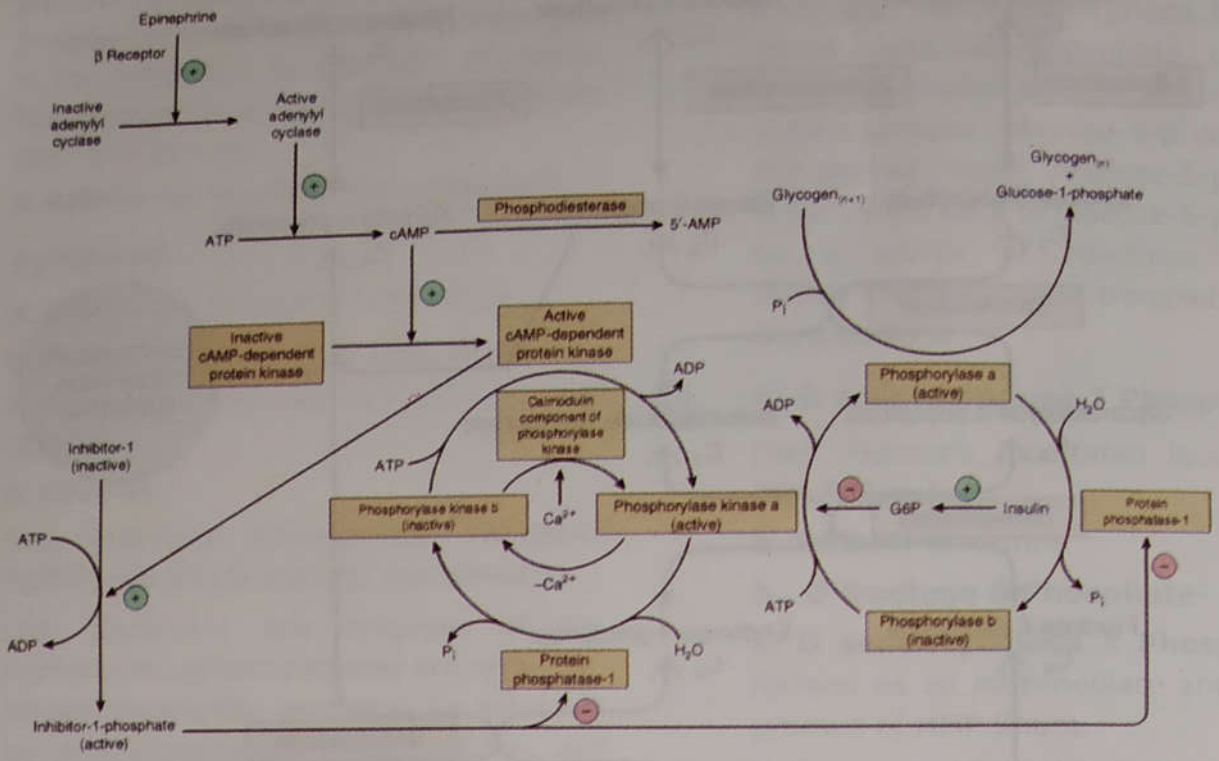
34. a) Contributing phosphate

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Contributing phosphate-

cAMP ACTIVATES GLYCOGEN PHOSPHORYLASE

Phosphorylase kinase is activated in response to cAMP. Increasing the concentration of cAMP activates cAMP-dependent protein kinase, which catalyzes the phosphorylation by ATP of inactive phosphorylase kinase b to active phosphorylase kinase a, which in turn, phosphorylates phosphorylase b to phosphorylase a. In the liver, cAMP is formed in response to glucagon, which is secreted in response to falling blood glucose. Muscle is insensitive to glucagon; in muscle, the signal for increased cAMP formation is the action of norepinephrine, which is secreted in response to fear or fright, when there is a need for increased glycogenolysis to permit rapid muscle activity.



b. Causing deposphorylation-by phosphorylation and not by dephosphorylation

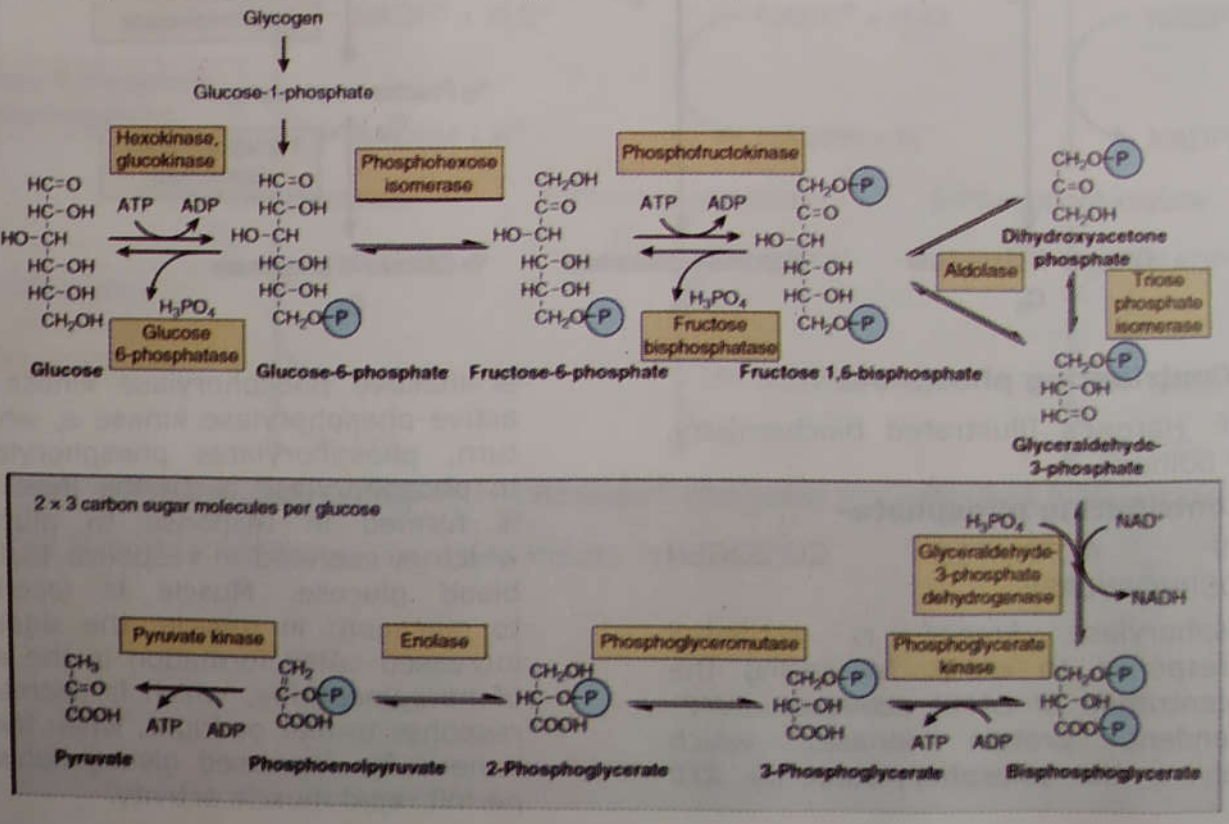
c. Uncoupling-this occurs in Chemiosmotic Theory of Electron transport chain coupled to oxidative phosphorylation , in presence of uncouplers.

d. All of the above

35. a) Invertase

36. d) Glycerophosphate dehydrogenase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

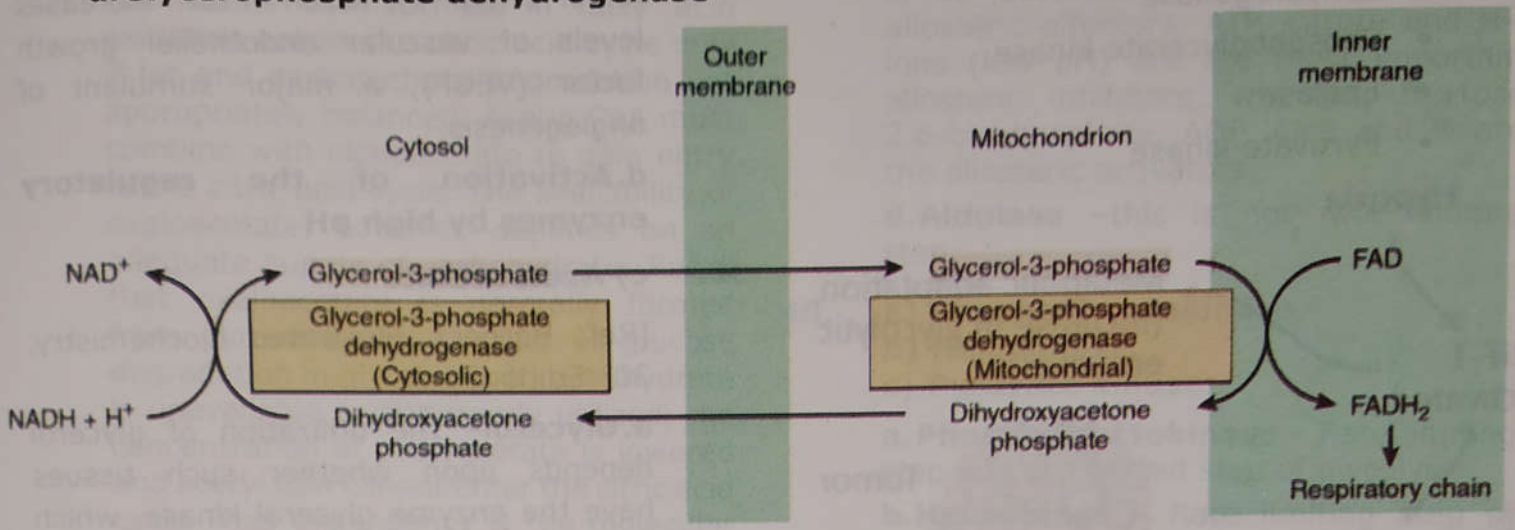


a. Enolase- is part of glycolysis.

b. Phosphoglyceromulase- is part of glycolysis.

c. Aldolase- is part of glycolysis.

d. Glycerophosphate dehydrogenase



Glycerophosphate shuttle for transfer of reducing equivalents from the cytosol into the mitochondrion.

37. c) Hypoxia stimulates release of all Glycolytic enzymes from band 3 on RBC membrane

a. hypoxia Stimulates pyruvate dehydrogenase by increased 2,3 DPG

b. Hypoxia inhibits hexokinase

c. Hypoxia stimulates release of all Glycolytic enzymes from band 3 on RBC membrane

Cancer cells display increased uptake of glucose, and glycolysis. As the tumors grow rapidly, the blood vessels are unable to supply adequate oxygen, and thus a condition of hypoxia exists. Due to this, anaerobic glycolysis predominantly occurs to supply energy. The cancer cells get adapted to hypoxic glycolysis through the involvement of a transcription factor namely hypoxia-inducible transcription factor (HIF). HIF increases the synthesis of glycolytic enzymes and the glucose transporters. However, the cancer cells cannot grow and survive without proper vascularization. One of the modalities of cancer treatment is to use drugs that can inhibit vascularization of tumors.

Hypoxia itself enhances tumor growth by activating a transcription factor, hypoxia-inducible transcription factor (HIF-1). HIF-1 increases the expression of most glycolytic enzymes and the glucose transporters GLUT1 and GLUT3 .

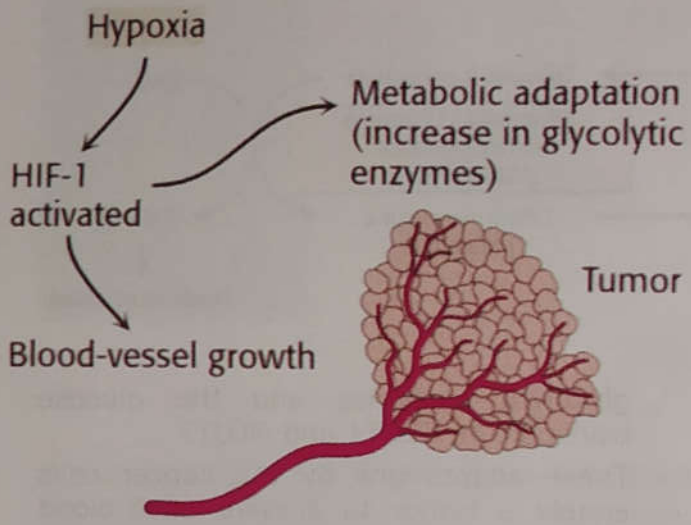
These adaptations by the cancer cells enable a tumor to survive until blood vessels can grow. HIF-1 also increases the expression of signal molecules, such as vascular endothelial growth f actor (VEGF), that facilitate the growth of blood vessels that will provide nutrients to the cells . Without new blood vessels, a tumor would cease to grow and either die or remain harmlessly small. Efforts are underway to develop drugs that inhibit the growth of blood vessels in tumors.

Hypoxia-inducible factors (HIFs): A family of transcription factors (at least three) important in directing cellular responses to varying levels of oxygen. Each factor is made up of a different oxygen-regulated α-subunit and a common constitutive β-subunit. At physiological levels of oxygen, the α-subunit undergoes rapid degradation, initiated by prolyl hydroxylases. HIFs have various functions; eg, HIF-1 up-regulates various genes encoding enzymes of glycolysis, and also the expression of vascular endothelial growth factor (VEGF).

Proteins in glucose metabolism encoded by genes regulated by hypoxia-inducible factors:

- GLUT1
- GLUT3
- Hexokinase

- Phosphofructokinase
- Aldolase
- Glyceraldehyde 3-phosphate dehydrogenase
- Phosphoglycerate kinase
- Enolase
- Pyruvate kinase



Alteration of gene expression in tumors owing to hypoxia.

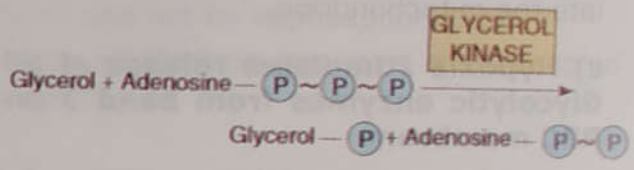
The growth of blood vessels supplying tumor cells can be stimulated by hypoxia and other factors. Hypoxia causes elevated levels of hypoxia-inducible factor-1 (HIF-1), which in turn increases levels of vascular endothelial growth factor (VEGF), a major stimulant of angiogenesis.

d. Activation of the regulatory enzymes by high pH

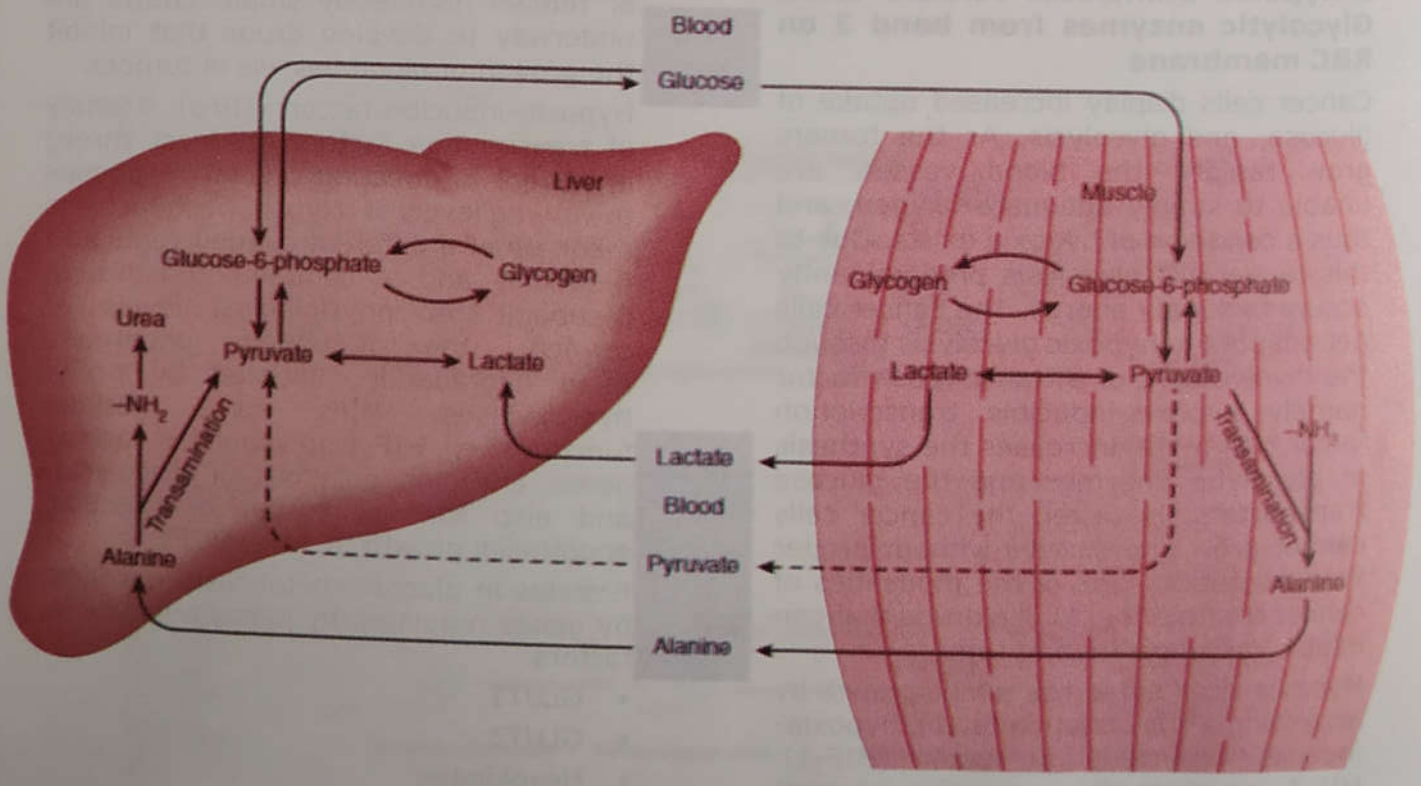
38. c) Acetoacetate

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Glycerol- The utilization of glycerol depends upon whether such tissues have the enzyme glycerol kinase, which is found in significant amounts in liver, kidney, intestine, brown adipose tissue, and the lactating mammary gland.



b. Alanine-



The lactic acid (Cori cycle) and glucose-alanine cycles.

c. Acetoacetate-gives acetyl CoA on complete combustion and hence does not give rise to glucose.

The acetyl CoA formed in fatty acid oxidation enters the citric acid cycle only if fat and carbohydrate degradation are appropriately balanced. Acetyl CoA must combine with oxaloacetate to gain entry to the citric acid cycle. The availability of oxaloacetate, however, depends on an adequate supply of carbohydrate. Recall that oxaloacetate is normally formed from pyruvate, the product of glucose degradation in glycolysis. If carbohydrate is unavailable or improperly utilized, the concentration of oxaloacetate is lowered and acetyl CoA cannot enter the citric acid cycle. This dependency is the molecular basis of the adage that FATS BURN IN THE FLAME OF CARBOHYDRATES.

d. Lactate-please refer to option b

39. c) Phosphofrutokinase

a. Hexokinase-

Hexokinase is inhibited by glucose 6-phosphate. This enzyme prevents the accumulation of glucose 6-phosphate due to product inhibition. This is rate limiting step.

b. Glucokinase- Glucokinase, which specifically phosphorylates glucose, is an inducible enzyme. The substrate glucose, probably through the involvement of insulin, induces glucokinase.

c. Phosphofrutokinase-

Phosphofruclokinase (PFK) is the most important regulatory enzyme in glycolysis. This enzyme catalyses the rate limiting committed step. PFK is an allosteric enzyme regulated by allosteric effectors. ATP, citrate and H+ ions (low pH) are the most important allosteric inhibitors, whereas, fructose 2,6-bisphosphate, ADP, AMP and Pi are the allosteric activators.

d. Aldolase –this is not rate limiting step.

40. a) Phosphofructokinase,
b) Hexokinase,
c) Pyruvate kinase

a. Phosphofructokinase - Rate limiting step and committed step of glycolysis.

b. Hexokinase - Rate limiting step of glycolysis.

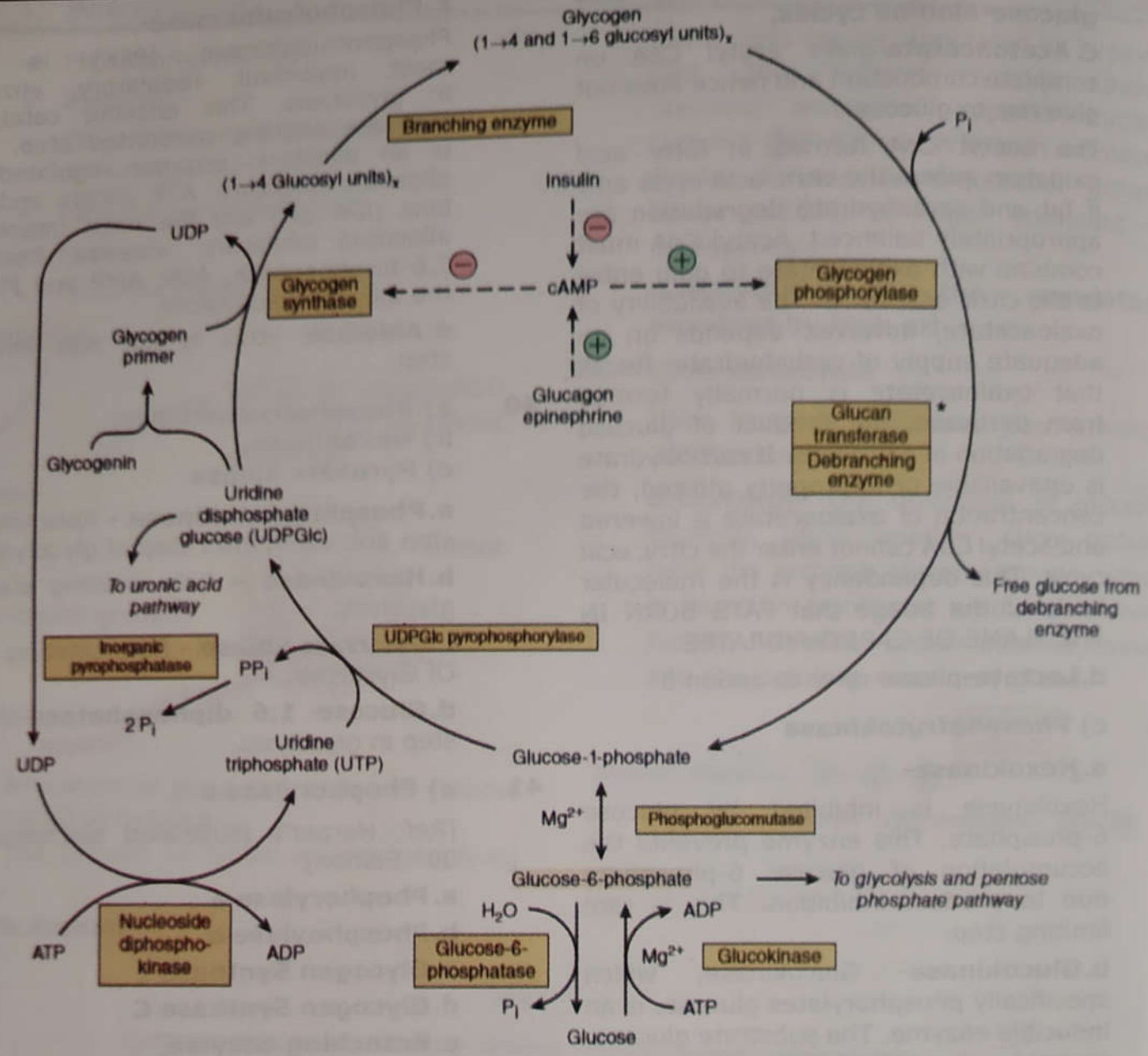
c. Pyruvate kinase - Rate Limiting Step Of Glycolysis.

d. Glucose 1.6 diphosphatase-Not a step in glycolysis.

41. a) Phophorylase a

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Phophorylase a
b. Phosphoylase b
c. Glycogen Synthase I
d. Glycogen Synthase C
e. Branching enzyme



42. e) Skin

a. Liver
b. Adipose tissue
c. Mammary gland
d. Skeletal muscle
e. Skin

Add a note on::::::

Pathways requiring NADPH Synthesis

- Fatty acid biosynthesis
- Cholesterol biosynthesis
- Neurotransmitter biosynthesis
- Nucleotide biosynthesis
- Detoxification Reduction of oxidized glutathione
- Cytochrome P450 monooxygenases

43. a) Glucose 6 phosphatase

a. Glucose 6 phosphatase- Skeletal muscle cannot contribute directly to blood glucose because it does not contain glucose-6-phosphatase.

Muscle glycogen cannot contribute directly to plasma glucose, since muscle lacks glucose-6-phosphatase, and the primary use of muscle glycogen is to provide a source of glucose-6-phosphate for energy-yielding metabolism in the muscle itself.

b. Hexokinase-is present in muscles.

c. Isomerase -is present in muscles.

d. Phosphofructokinase-is present in muscles.

44. d) Condensation

[Ref: Stryer 8th Edition]

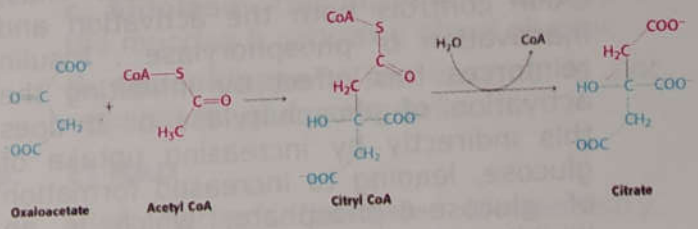
a. Hydration

b. Deacylation

c. Dehydrogenation

d. Condensation-

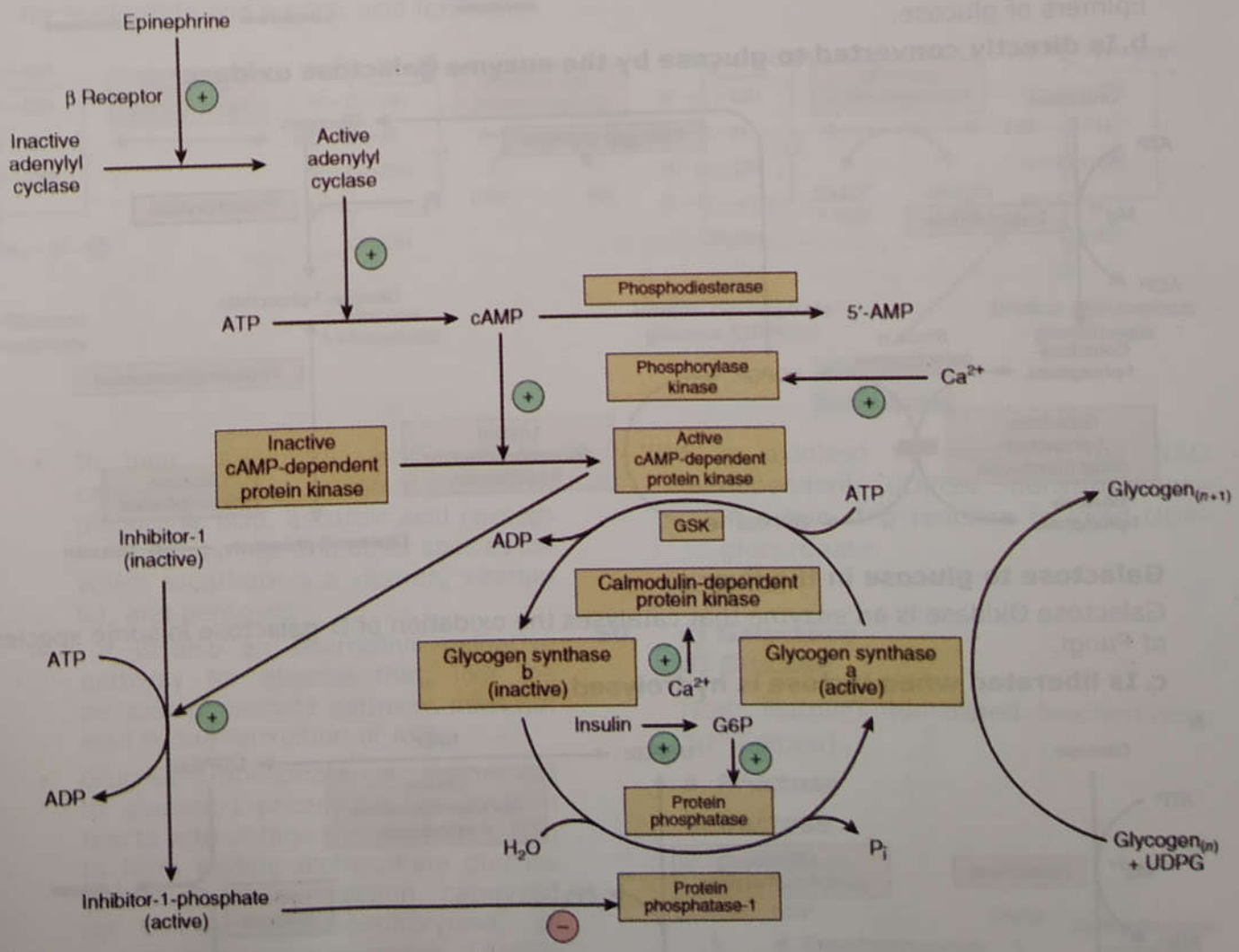
The citric acid cycle begins with the condensation of a four-carbon unit, oxaloacetate, and a two-carbon unit, the acetyl group of acetyl CoA. Oxaloacetate reacts with acetyl CoA and H2O to yield citrate and CoA. This reaction, which is an aldol condensation followed by a hydrolysis, is catalyzed by citrate synthase. Oxaloacetate first condenses with acetyl CoA to form citryl CoA, a molecule that is energy rich because it contains the thioester bond that originated in acetyl CoA. The hydrolysis of citryl CoA thioester to citrate and CoA drives the overall reaction far in the direction of the synthesis of citrate. In essence, the hydrolysis of the thioester powers the synthesis of a new molecule from two precursors.



45. b) Insulin

a. Cortisone

b. Insulin-



Control of glycogen synthase in muscle.

Protein Phosphatase-1 Inactivates Glycogen Phosphorylase

Both phosphorylase a and phosphorylase kinase a are dephosphorylated and inactivated by protein phosphatase-1. Protein phosphatase-1 is inhibited by a protein, inhibitor-1, which is active only after it has been phosphorylated by cAMP-dependent protein kinase. Thus, cAMP controls both the activation and inactivation of phosphorylase . Insulin reinforces this effect by inhibiting the activation of phosphorylase b. It does this indirectly by increasing uptake of glucose, leading to increased formation of glucose-6-phosphate, which is an inhibitor of phosphorylase kinase.

c. Lactate

d. Ethanol

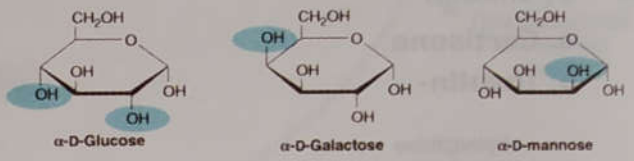
46. a) Has the same molecular weight as glucose
c) Is liberated when lactose is hydrolysed
e) In the urine gives a positive test with clinitest tablets

[Ref: Stryer 8th Edition & Harper's Illustrated biochemistry, 30th Edition]

a. Has the same molecular weight as glucose-

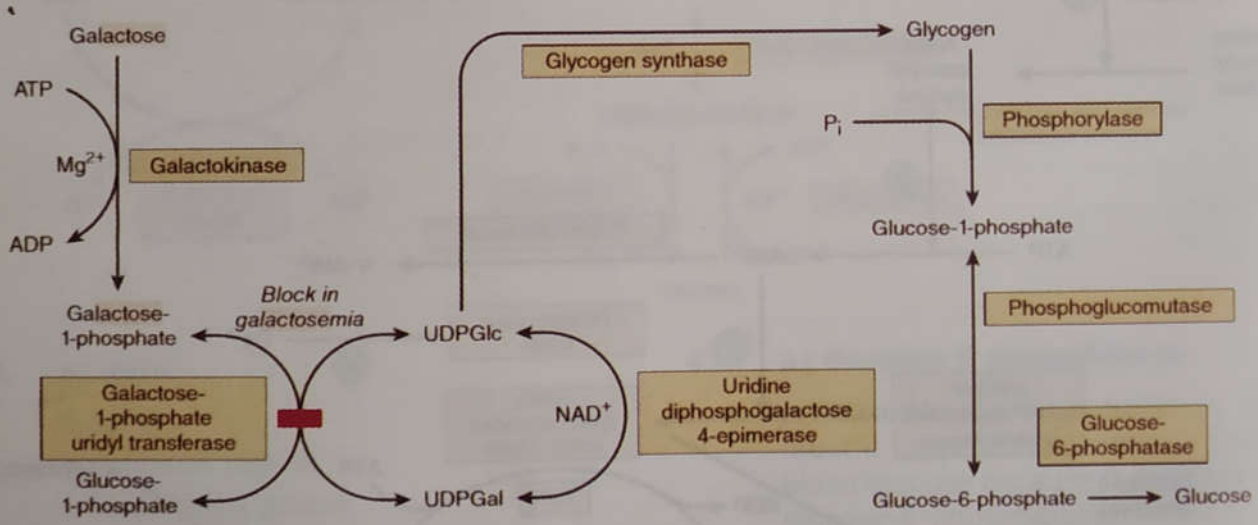
Glucose, galactose, fructose, and mannose are physiologically the most important hexoses .The biochemically important ketoses and aldoses.

Glucose and Galactose have same molecular weight.



Epimers of glucose.

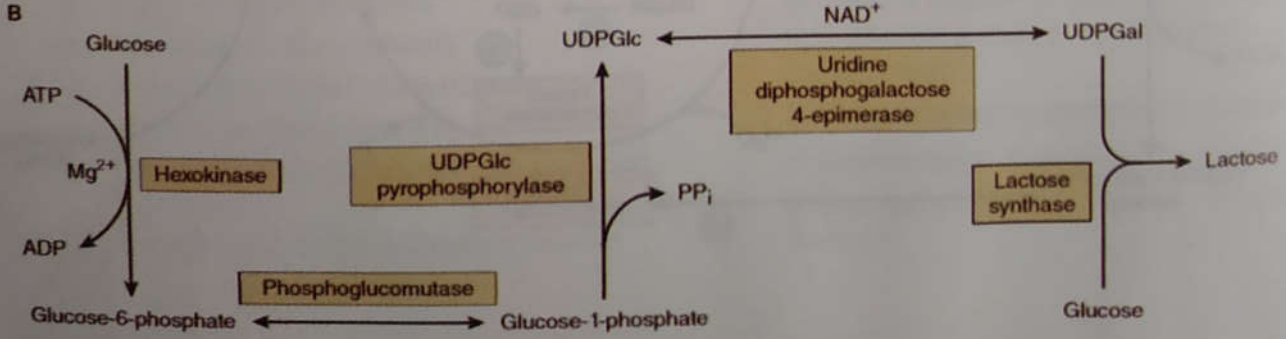
b. Is directly converted to glucose by the enzyme galactose oxidase-



Galactose to glucose in the liver

Galactose Oxidase is an enzyme that catalyses the oxidation of D-galactose in some species of Fungi.

c. Is liberated when lactose is hydrolysed –



Glucose to lactose in the lactating mammary gland.

d. From the diet is stored in the liver as galactose 1-phosphate-

Galctose is finally stored as glycogen.

e. In the urine gives a positive test with clinitest tablets-

Clinitest is based on benedict's reduction reaction and is given positive by redicing substances.

47. c) NADPH

a. FAD

b. NAD

c. NADPH -

The pentose phosphate pathway is an alternative route for the metabolism of glucose. It does not lead to formation of ATP but has two major functions: (1) the formation of NADPH for synthesis of fatty acids and steroids and maintaining reduced glutathione for antioxidant activity, and (2) the synthesis of ribose for nucleotide and nucleic acid formation.

d. FMN

48. b) G – 6-phosphatase

G-6-P dehydrogenase – This enzyme is not required for gluconeogensis.

b. G – 6-phosphatase-

Skeletal muscle cannot contribute directly to blood glucose because it does not contain glucose-6-phosphatase.

c. Aldolase- This enzyme is present in the muscles & can raise blood glucose

d. Glucokinase- This enzyme is not required for gluconeogensis.

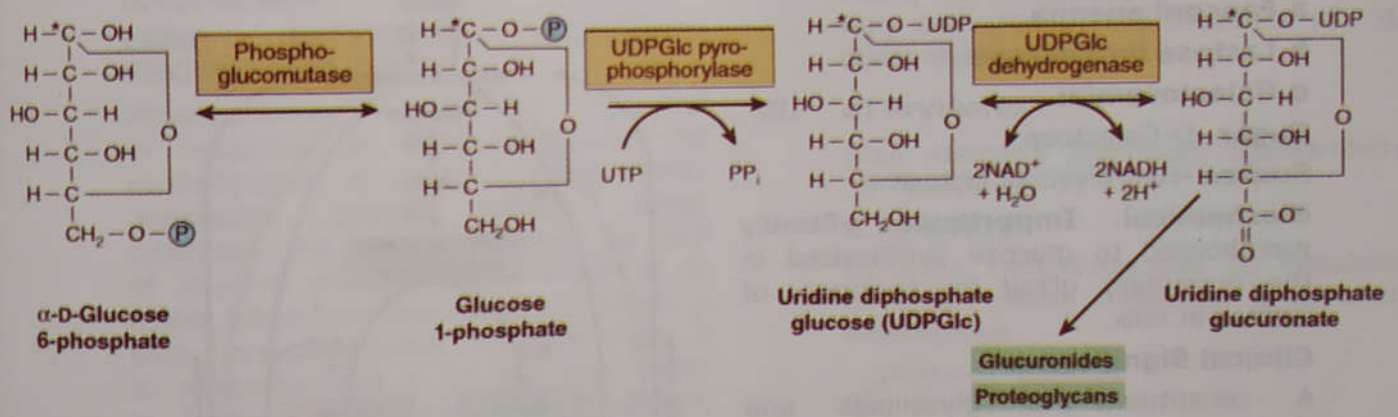
49. c) NAD

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. ATP

b. FAD

c. NAD



- In liver, the uronic acid pathway catalyzes the conversion of glucose to glucuronic acid, ascorbic acid (except in human beings and other species for which ascorbate is a vitamin, vitamin C), and pentoses .
- It is also an alternative oxidative pathway for glucose that, like the pentose phosphate pathway, does not lead to the formation of ATP.
- Glucose-6-phosphate is isomerized to glucose-1-phosphate, which then reacts with uridine triphosphate (UTP) to form uridine diphosphate glucose (UDPGlc) in a reaction catalyzed by UDPGlc pyrophosphorylase, as occurs in glycogen synthesis. UDPGlc is oxidized at carbon 6 by NAD dependent UDPGlc dehydrogenase in a two-step reaction to yield UDP-glucuronate.

d. NADP

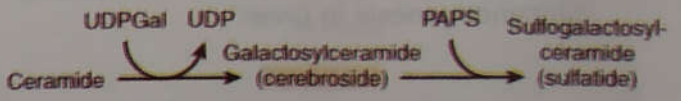
50. c) Galactose
d) Glucose

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Fructose

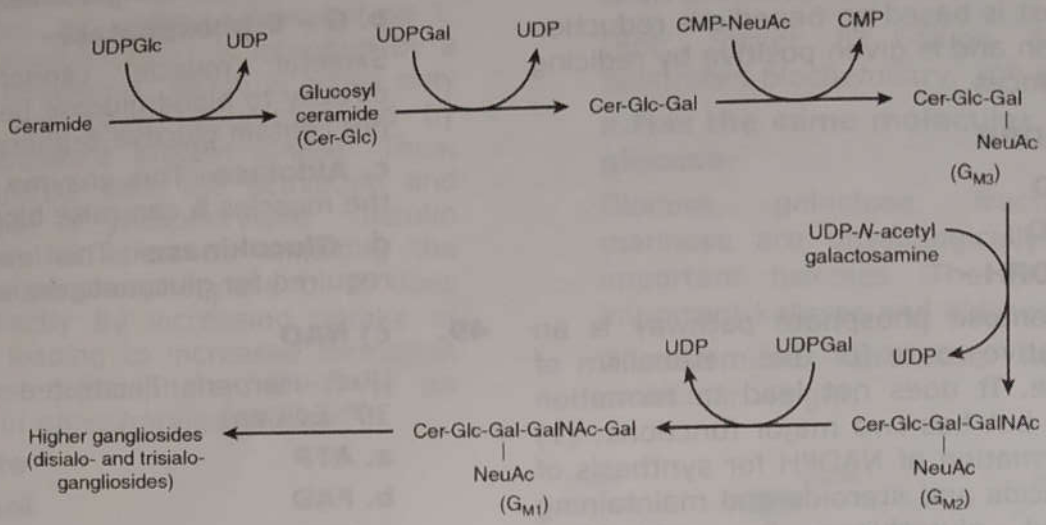
b. Sucrose

c. Galactose



The simplest glycosphingolipids (cerebrosides) are galactosylceramide (GalCer) and glucosylceramide (GlcCer). GalCer is a major lipid of myelin, whereas GlcCer is the major glycosphingolipid of extraneural tissues and a precursor of most of the more complex glycosphingolipids.

d. Glucose



Biosynthesis of gangliosides.

51. c) Galactosemia

a. Fanconi anemia

b. Lactose intolerance

c. Galactosemia:

Sugar -D-Galactose

Source -Hydrolysis of lactose

Biochemical Importance -Readily metabolized to glucose synthesized in the mammary gland for synthesis of lactose in milk.

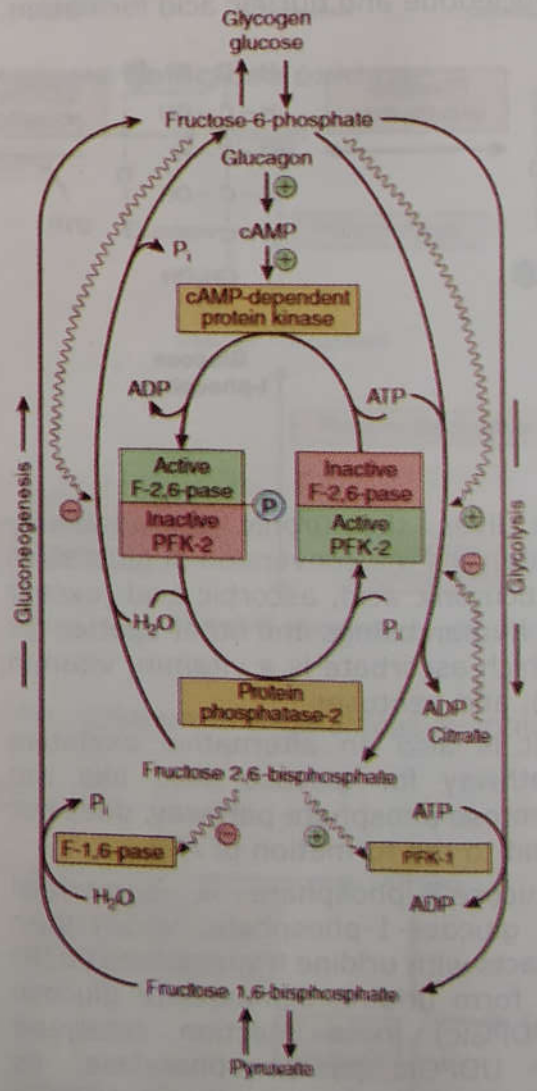
Clinical Significance-

A constituent of glycolipids and glycoproteins

Hereditary galactosemia as a result of failure to metabolize galactose leads to cataracts.

d. Phenylketonuria

e. Salicylate poisoning



52. b) Liver

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Brain

b. Liver -

Fructose 2,6-Bisphosphate Plays a Unique Role in the Regulation of Glycolysis & Gluconeogenesis in Liver

c. Adrenal Cortex

d. RBC

e. Muscle

53. a) A hemiacetal

a. A hemiacetal -

Benedict's test : This is a test for the identification of reducing sugars, which form enediols (predominantly under alkaline conditions). The enediol forms of sugars reduce cupric ions (Cu2+) of copper sulfate to cuprous ions (Cu+) which form a yellow precipitate of cuprous hydroxide or a red precipitate of cuprous oxide.

b. Cupric ions

c. A free carboxy

d. A free hydroxyl

54. b) Blood glucose

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Cyclic AMP -

cAMP ACTIVATES GLYCOGEN PHOSPHORYLASE

Phosphorylase kinase is activated in response to cAMP.Increasing the concentration of cAMP activates cAMP-dependent protein kinase, which catalyzes the phosphorylation by ATP of inactive phosphorylase kinase b to active phosphorylase kinase a, which in turn, phosphorylates phosphorylase b to phosphorylase a. In the liver, cAMP is formed in response to glucagon, which is secreted in response to falling blood glucose. Muscle is insensitive to glucagon; in muscle, the signal for increased cAMP formation is the action of norepinephrine, which is secreted in response to fear or fright, when there is a need for increased glycogenolysis to permit rapid muscle activity.

b. Blood glucose-inhibits glycogen breakdown

c. Epinephrine-

Phosphorylation is increased in response to cyclic AMP (cAMP) formed from ATP by adenylyl cyclase at the inner surface of cell membranes in response to hormones such as epinephrine, norepinephrine, and glucagon. cAMP is hydrolyzed by phosphodiesterase, so terminating hormone action; in liver insulin increases the activity of phosphodiesterase.

d. Calcium-

Ca2+ Synchronizes the Activation of Glycogen Phosphorylase

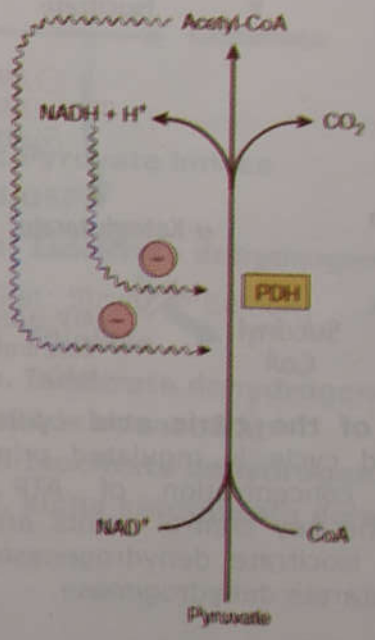
With Muscle Contraction Glycogenolysis in muscle increases several hundred-fold at the onset of contraction; the same signal (increased cytosolic Ca2+ ion concentration) is responsible for initiation of both contraction and glycogenolysis. Muscle phosphorylase kinase, which activates glycogen phosphorylase, is a tetramer of four different subunits, α, β, γ, and δ. The α and β subunits contain serine residues that are phosphorylated by cAMP-dependent protein kinase. The δ subunit is identical to the Ca^{2+}-binding protein calmodulin, and binds four Ca^{2+}. The binding of Ca^{2+} activates the catalytic site of the γ subunit even while the enzyme is in the dephosphorylated b state; the phosphorylated a form is only fully activated in the presence of high concentrations of Ca^{2+}.

55. a) Pryuvate

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Pyruvate

Pyruvate Dehydrogenase Is Regulated by End-Product Inhibition & Covalent Modification



The cycle starts with reaction between the acetyl moiety of acetyl-CoA and the four-carbon dicarboxylic acid oxaloacetate, forming a six-carbon tricarboxylic acid, citrate. In the subsequent reactions, two molecules of CO2 are released and oxaloacetate is regenerated.Only a small quantity of oxaloacetate is needed for the oxidation of a large quantity of acetyl-CoA; it can be considered as playing a catalytic role, since it is regenerated at the end of the cycle.

b. Glycine

c. HCL

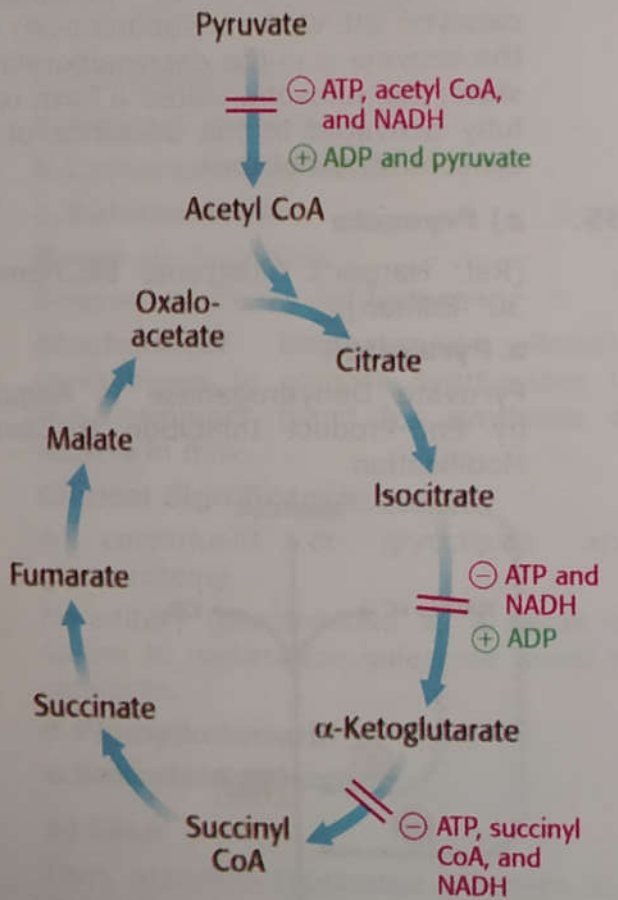
d. Lipoprotein

56. b) Alpha ketoglutarate

[Ref: Stryer 8th Edition]

a. Citrate -aconitase is not rate limiting step.

b. Alpha ketoglutarate –



Control of the citric acid cycle-The citric acid cycle is regulated primarily by the concentration of ATP and NADH. The key control points are the enzymes isocitrate dehydrogenase and a-ketoglutarate dehydrogenase.

The rate of the citric acid cycle is precisely adjusted to meet an animal cell's needs for ATP .The primary control points are the allosteric enzymes isocitrate dehydrogenase and a-ketoglutarate dehydrogenase.

c. Succinate -Succinyl CoA synthetase is not rate limiting step.

d. Malate -Fumarase is not rate limiting step.

57. a) 10

a. 10- ten ATP are formed per turn of the citric acid cycle.

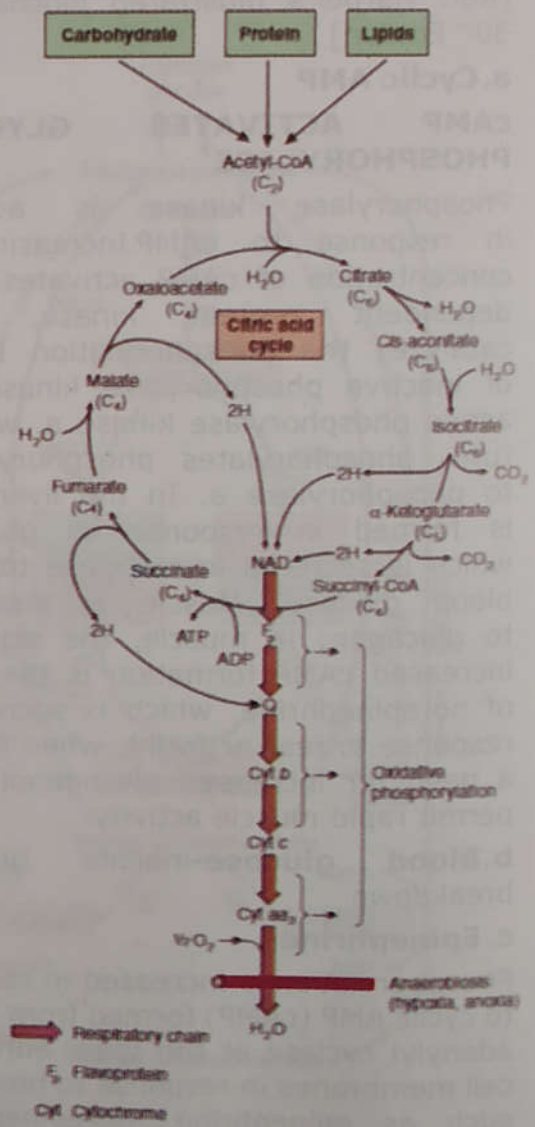
b. 11

c. 12

d. 15

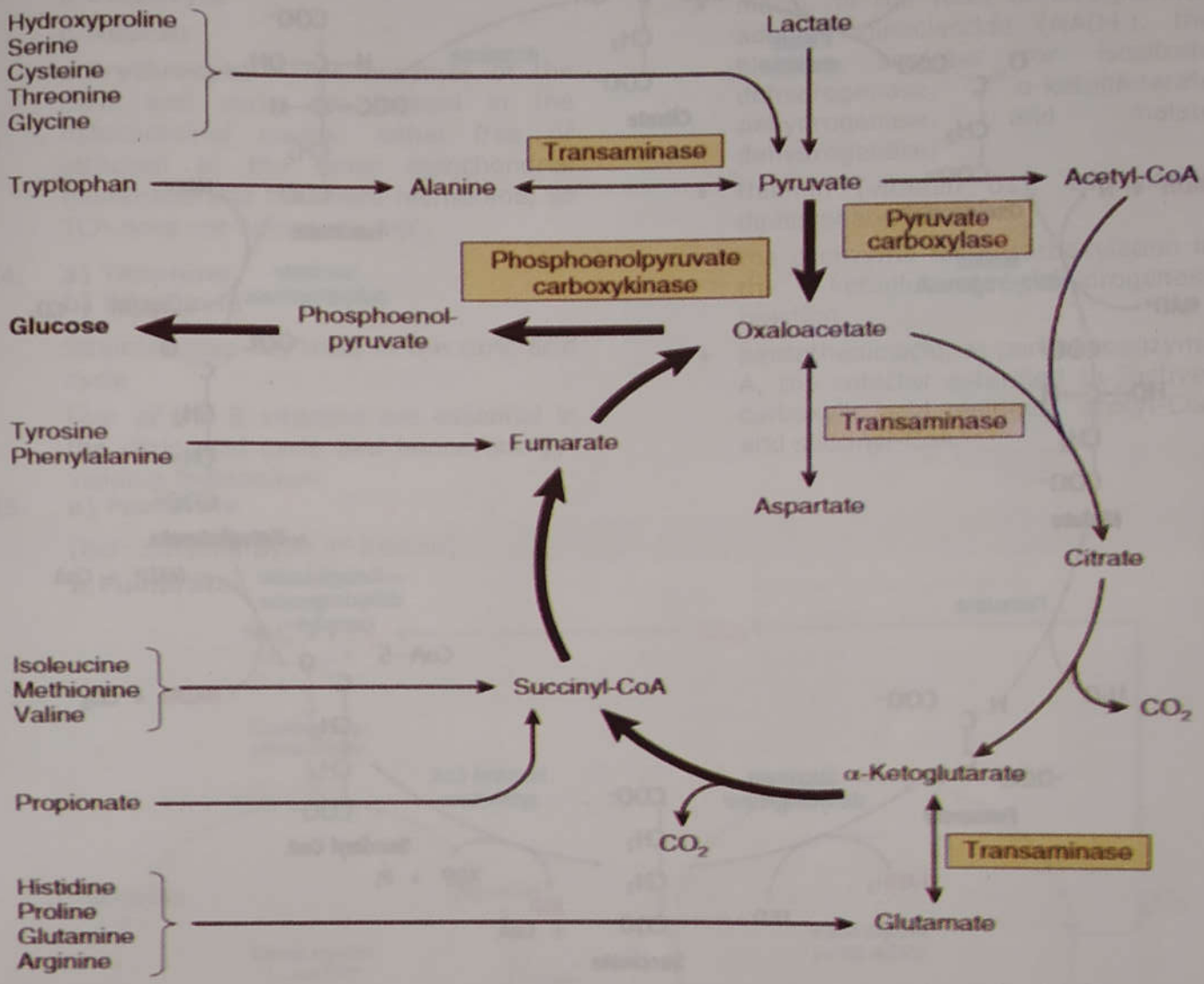
58. d) Citric acid cycle

[Ref: Harper's Illustrated biochemistry, 30th Edition]



59. c) Succinyl CoA

[Ref: Harper's Illustrated biochemistry, 30th Edition]



60. a) Pyruvate carboxylase

a. Pyruvate carboxylase

One of the most important of such anaplerotic reactions is the formation of oxaloacetate by the carboxylation of pyruvate, catalyzed by pyruvate carboxylase. This reaction is important in maintaining an adequate concentration of oxaloacetate for the condensation reaction with acetylCoA.

b. Enolase

c. Pyruvate kinase

d. G6PD

61. b) Isocitrate dehydrogenase

[Ref: Stryer 8th Edition]

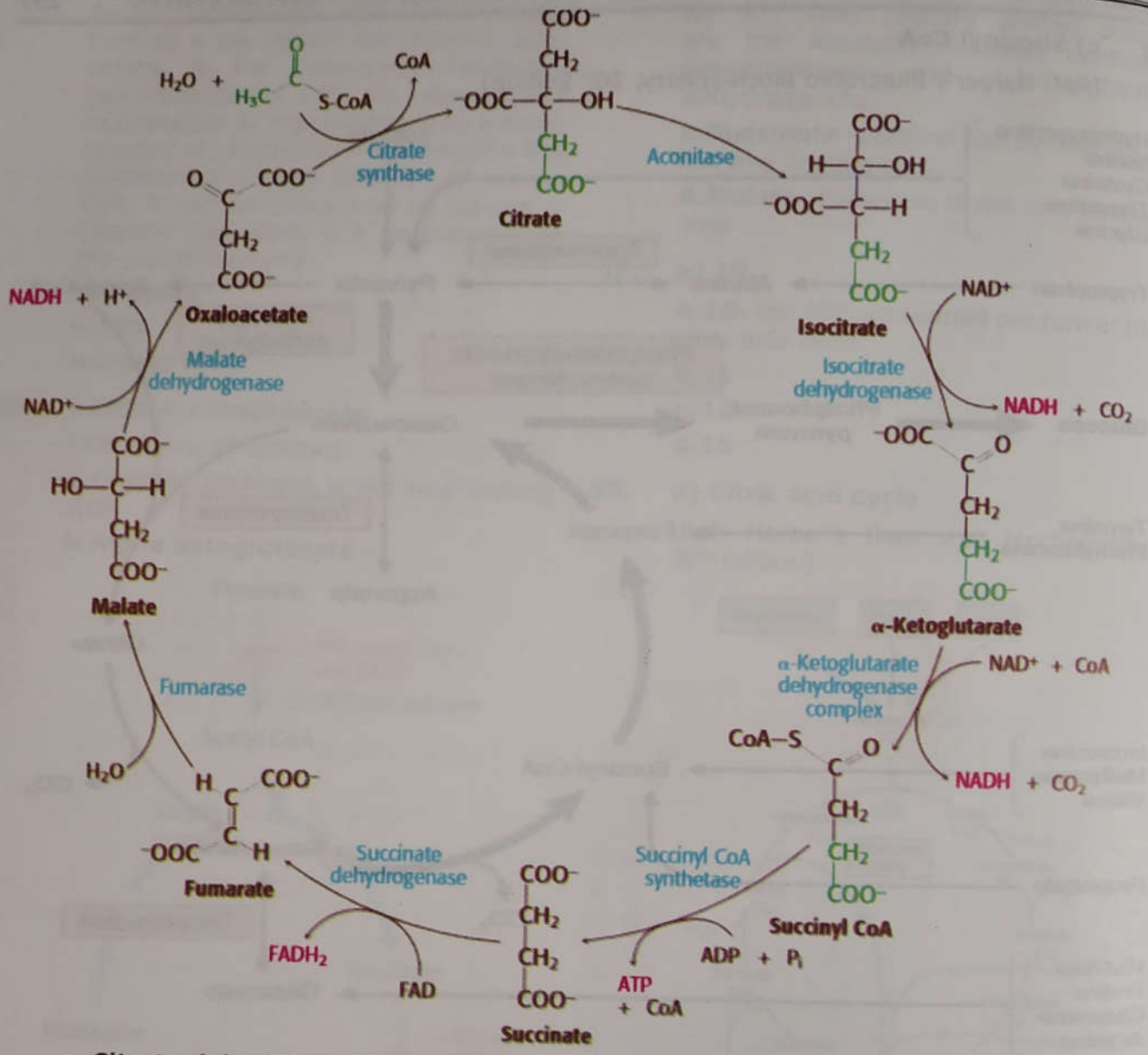
a. Thiolase

b. Isocitrate dehydrogenase

CO2 is released at

1. Isocitrate dehydrogenase

2. alpha ketoglurate dehydrogenase



c. Citrate dehydrogenase

d. alpha ketoglurate

62. b) Succinate thiokinase

[Ref: Stryer 8th Edition]

a. Alpha keto glutarate dehydrogenase

b. Succinate thiokinase -Succinyl-CoA is converted to succinate by the enzyme succinate thiokinase (succinyl-CoA synthetase). This is the only example of substrate level phosphorylation in the citric acid cycle. Tissues in which gluconeogenesis occurs (the liver and kidney) contain two isoenzymes of succinate thiokinase, one specific for GDP and the other for ADP. The GTP formed is used for the decarboxylation of oxaloacetate to phosphoenolpyruvate in gluconeogenesis, and provides a regulatory link between citric acid cycle activity and the withdrawal of oxaloacetate for gluconeogenesis. Nongluconeogenic tissues have only the isoenzyme that phosphorylates ADP.

c. Isocitrate dehydrogenase

d. Fumarase

e. Malate dehydrogenase

63. d) Erythrocyte

a. Hepatocyte

b. Osteocyte

c. Neuron

d. Erythrocyte - The enzymes of the citric acid cycle are located in the mitochondrial matrix, either free or attached to the inner mitochondrial membrane and the crista membrane, so TCA does not operate in RBC.

64. a) Thiamine
b) Riboflavin

Vitamins play key roles in the citric acid cycle

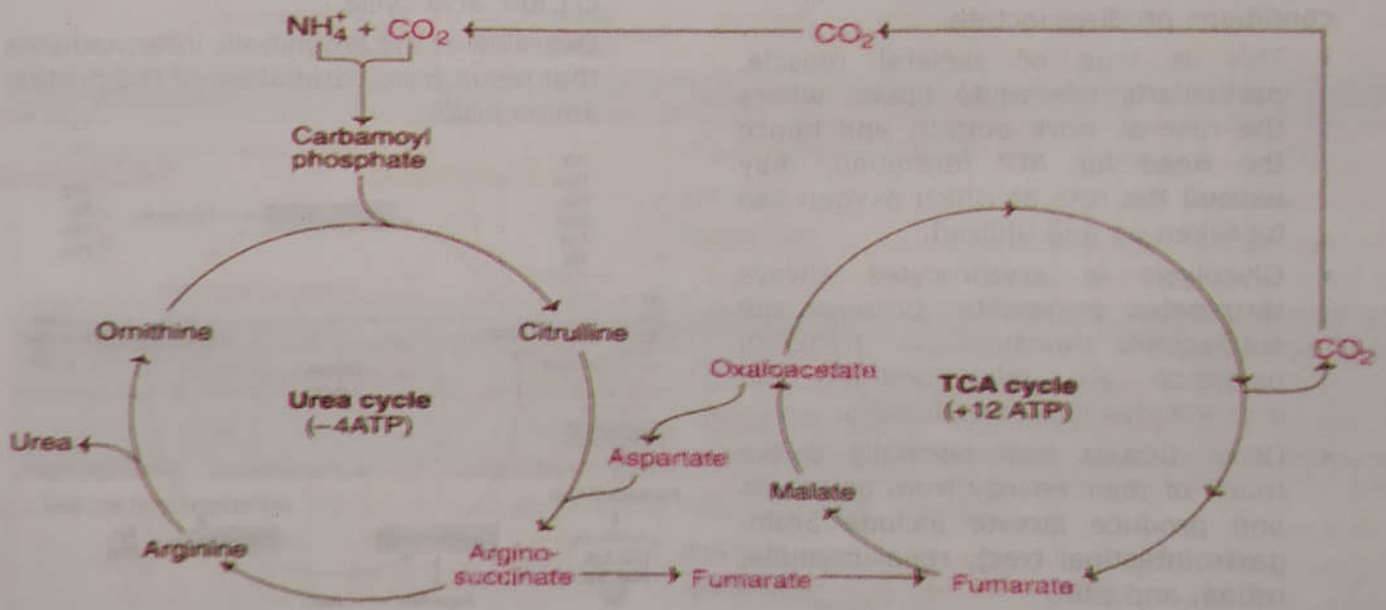
Four of the B vitamins are essential in the citric acid cycle and hence energy-yielding metabolism:

- riboflavin, in the form of flavin adenine dinucleotide (FAD), a cofactor for succinate dehydrogenase;
- niacin, in the form of nicotinamide adenine dinucleotide (NAD+), the electron acceptor for isocitrate dehydrogenase, α-ketoglutarate dehydrogenase, and malate dehydrogenase;
- thiamin (vitamin B1), as thiamin diphosphate,
- the coenzyme for decarboxylation in the α-ketoglutarate dehydrogenase reaction;
- pantothenic acid, as part of coenzyme A, the cofactor esterified to "active" carboxylic acid residues: acetyl-CoA and succinyl-CoA.

65. a) Fumarate

[Ref: Satyanarayan 4th Edition]

a. Fumarate



The production of fumarate in urea cycle is the most important integrating point with TCA cycle. Fumarate is converted to malate and then to oxaloacetate in TCA cycle. Oxaloacetate undergoes transamination to produce aspartate which enters urea cycle. Here, it combines with citrulline to produce arginosuccinate. Oxaloacetate is an important metabolite which can combine with acetyl CoA to form citrate and get finally oxidized. Oxaloacetate can also serve as a precursor for the synthesis of glucose (gluconeogenesis).

b. Sucinate

c. Oxaloacetale

d. Arginino sucinate

66. a) 100 mg%

a. 100 mg%

b. 140 mg%

c. 180 mg%

When the blood glucose concentration rises above about 10 mmol /L, the kidney also exerts a (passive) regulatory effect. Glucose is continuously filtered by the glomeruli, but is normally completely reabsorbed in the renal tubules by active transport. The capacity of the tubular system to reabsorb glucose is limited to a rate of about 2 mmol/min, and in hyperglycemia (as occurs in poorly controlled diabetes mellitus), the glomerular filtrate may contain more glucose than can be reabsorbed, resulting in glucosuria when the renal threshold for glucose is exceeded. Presence of glucose in urine is usually seen when plasma glucose rises above the renal threshold of ~180 mg/dL.

d. 80 mg%

67. b) Lactate-

a. Pyruvate

b. Lactate-

Tissues that function under hypoxic conditions produce lactate

- This is true of skeletal muscle, particularly the white fibers, where the rate of work output, and hence the need for ATP formation, may exceed the rate at which oxygen can be taken up and utilized.
- Glycolysis in erythrocytes always terminates in lactate, because the subsequent reactions of pyruvate oxidation are mitochondrial, and erythrocytes lack mitochondria.
- Other tissues that normally derive much of their energy from glycolysis and produce lactate include brain, gastrointestinal tract, renal medulla, retina, and skin.
- Lactate production is also increased in septic shock, and many cancers also produce lactate.
- The liver, kidneys, and heart normally take up lactate and oxidize it, but produce it under hypoxic conditions.
- When lactate production is high, as in vigorous exercise, septic shock, and cancer cachexia, much is used in the liver for gluconeogenesis, leading to an increase in metabolic rate to provide the ATP and GTP needed. The increase in oxygen consumption as a result of increased oxidation of metabolic fuels to provide the ATP and GTP needed for gluconeogenesis is seen as oxygen debt after vigorous exercise.
- Under some conditions, lactate may be formed in the cytosol, but then enter the mitochondrion to be oxidized to pyruvate for onward metabolism. This provides a pathway for the transfer of reducing equivalents from the cytotol into the mitochondrion for the electron transport chain in addition to the glycerophosphate & malate-aspartate shuttles.

c. 2,3-bisphosphoglycerate

d. 3-phosphoglycerate

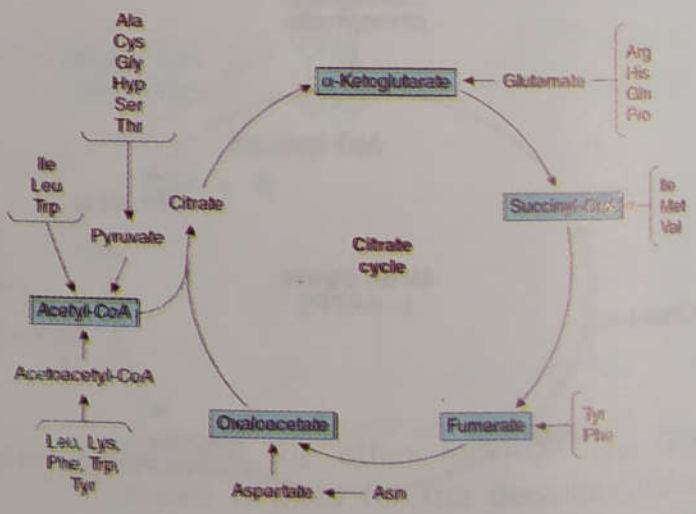
68. a) Glycolysis

a. Glycolysis

b. Beta oxidation

c. Citric acid cycle

Overview of the amphibolic intermediates that result from catabolism of the protein amino acids:



d. Alpha – oxidation

69. b) Maltose

a. Mannose

b. Maltose

Glucose is generated from dietary carbohydrates

- We typically consume in our diets a generous amount of starch and a s maller amount of glycogen. These complex carbohydrates must be

converted into simpler carbohydrates for absorption by the intestine and transport in the blood.

- Amylopectin, amylose, and glycogen are rapidly hydrolyzed by alpha-amylase, an enzyme secreted by the salivary glands and the pancreas.
- Starch and glycogen are digested primarily by the pancreatic enzyme alpha amylase and to a lesser extent by salivary amylase.
- Amylase cleaves the alpha-1,4 bonds of starch and glycogen, but not the a-1,6 bonds.
- The products are the di- and trisaccharides maltose and maltotriose.

c. sucrose

d. Fructose

70. a) Fructose 1, 6 bisphosphatase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Fructose 1, 6 bisphosphatase

b. Glucokinase

c. Fructokinase

d. None

Thermodynamic Barriers Prevent a Simple Reversal of Glycolysis

Three non equilibrium reactions in glycolysis, catalyzed by

- **hexokinase**
- **phosphofructokinase**
- **pyruvate kinase**

Prevent simple reversal of glycolysis for glucose synthesis.

They are circumvented as follows:

Activity In	Carbohydrate	Fasting and Feeding Diabetes	Inducer	Repressor	Activator	Inhibitor
Gluconeogenesis						
Pyruvate carboxylase	↓	↑	Glucocorticoids, glucagon, epinephrine	Insulin	Acetyl CoA	ADP
Phosphoenolpyruvate carboxykinase	↓	↑	Glucocorticoids, glucagon, epinephrine	Insulin	Glucagon	
Glucose 6-phosphatase	↓	↑	Glucocorticoids, glucagon, epinephrine	Insulin		

71. c) Nucleoside diphosphate kinase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

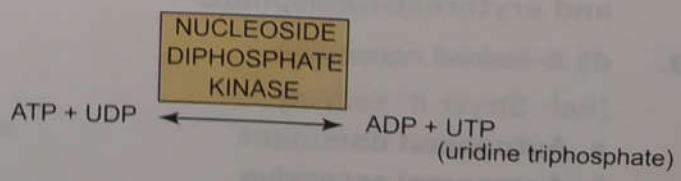
a. Pyruvate carboxykinase

b. Succinate thiokinase

c. Nucleoside diphosphate kinase

Other Nucleoside Triphosphates Participate in the Transfer of High-Energy Phosphate:

By means of the nucleoside diphosphate (NDP) kinases, UTP, GTP, and CTP can be synthesized from their diphosphate, for example, UDP reacts with ATP to form UTP.



All of these triphosphates take part in phosphorylations in the cell. Similarly, specific nucleoside monophosphate (NMP) kinases catalyze the formation of nucleoside diphosphates from the corresponding monophosphates. Thus, adenylate kinase is a specialized NMP kinase.

d. None of the above

72. a) Transfers two carbon fragments to an aldehyde acceptor

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Transfers two carbon fragments to an aldehyde acceptor

Transketolase transfers the two-carbon unit comprising carbons 1 and 2 of a ketose onto the aldehyde carbon of an aldose sugar. It therefore effects the conversion of a ketose sugar into an aldose with two carbons less and an aldose sugar into a ketose with two carbons more. The reaction requires Mg2+ and thiamin diphosphate (vitamin B1) as coenzyme. Measurement of erythrocyte transketolase and its activation by thiamin diphosphate provides an index of vitamin B1 nutritional status.The two-carbon moiety transferred is probably glycolaldehyde bound to thiamin diphosphate. Thus, transketolase catalyzes the transfer of the two-carbon unit from xylulose-5-phosphate to ribose-5-phosphate, producing the seven-carbon ketose sedoheptulose-7-phosphate and the aldose glyceraldehyde-3-phosphate. These two products then undergo transaldolation.

b. Transfers a three carbon Ketone containing fragments to an acceptor-

c. Converts ribose5 phophate to xylulose 5phosphate-

d. Concerts two five carbon sugar phosphates to fructose6phosphate and erythrose4phosphate-

73. d) X-linked recessive

[Ref: Stryer 8th Edition]

a. Autosomal dominant

b. Autosomal recessive

c. X-linked dominant

d. X-linked recessive

Deficiency of glucose 6-phosphate dehydrogenase, the enzyme catalyzing the first step in the oxidative branch of the pentose phosphate pathway. The result is a dearth of NADPH in all cells, but this deficiency is most acute in red blood cells. This defect, which is inherited on the X chromosome, is the most common disease that results from an enzyme malfunction, affecting hundreds of millions of people.

Peroxides are normally eliminated by the enzyme glutathione peroxidase, which uses reduced glutathione as a reducing agent.

$$2\,GSH + ROOH \xrightarrow{\text{Glutathione peroxidase}} GSSG + H_2O + ROH$$

In the absence of glucose 6-phosphate dehydrogenase, peroxides continue to damage membranes because no NADPH is being produced to restore reduced glutathione. Reduced glutathione is also essential for maintaining the normal structure of red blood cells by maintaining the structure of hemoglobin. The reduced form of glutathione serves as a sulfhydryl buffer that keeps the residues of hemoglobin in the reduced sulfhydryl form. Without adequate levels of reduced glutathione, the hemoglobin sulfhydryl groups can no longer be maintained in the reduced form. Hemoglobin molecules then cross-link with one another to form aggregates called Heinz bodies on cell membranes.

74. a) Ligase

a. Ligase-enzymes that catalyze the joining together (ligation) of two molecules in reactions coupled to the hydrolysis of ATP.

b. Transferase- enzymes that catalyze transfer of moieties such as glycosyl, methyl, or phosphoryl groups. The IUB name of hexokinase is ATP:D-hexose 6-phosphotransferase E.C. 2.7.1.1. This name identifies hexokinase as a member of class 2 (transferases), subclass 7 (transfer of a phosphoryl group), sub-subclass 1 (alcohol is the phosphoryl acceptor), and "hexose-6" indicates that

the alcohol phosphorylated is on carbon six of a hexose. Despite their clarity, IUB names are lengthy and relatively cumbersome, so we generally continue to refer to hexokinase and many other enzymes by their traditional, albeit sometimes ambiguous names. On the other hand E.C. numbers are particularly useful to differentiate enzymes with similar functions or catalytic activities.

c. Oxidoreductase - enzymes that catalyze oxidations and reductions.

d. Reductase- enzymes that catalyze reductions.

75. c) Fructokinase

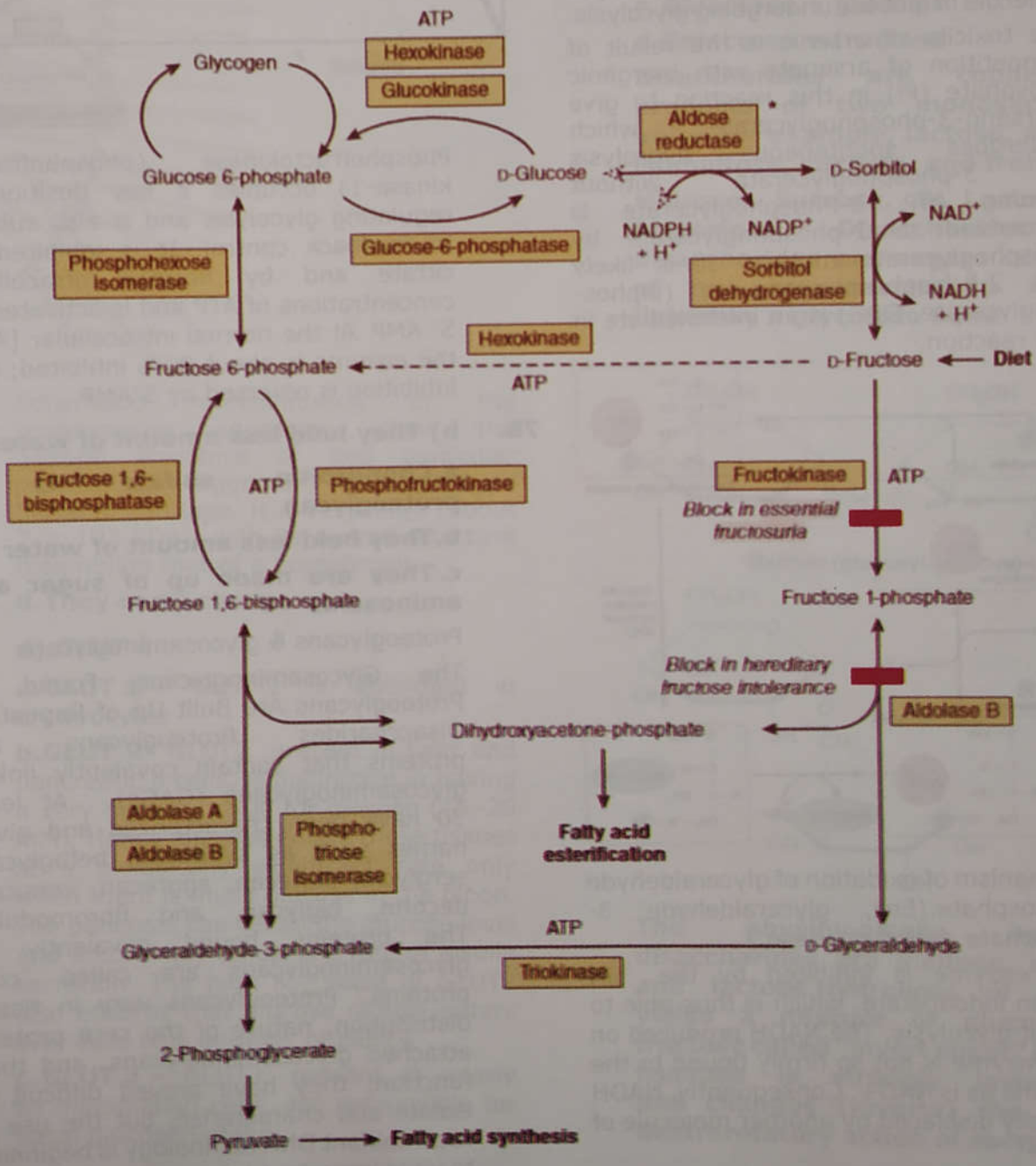
[Ref: Harper's Illustrated biochemistry, 30th Edition

a. Beta-galactosidase

b. Aldolase-B

c. Fructokinase

Defects in Fructose Metabolism Cause Disease



d. Aldose reductase

76. c) Phosphoglycerate Kinase

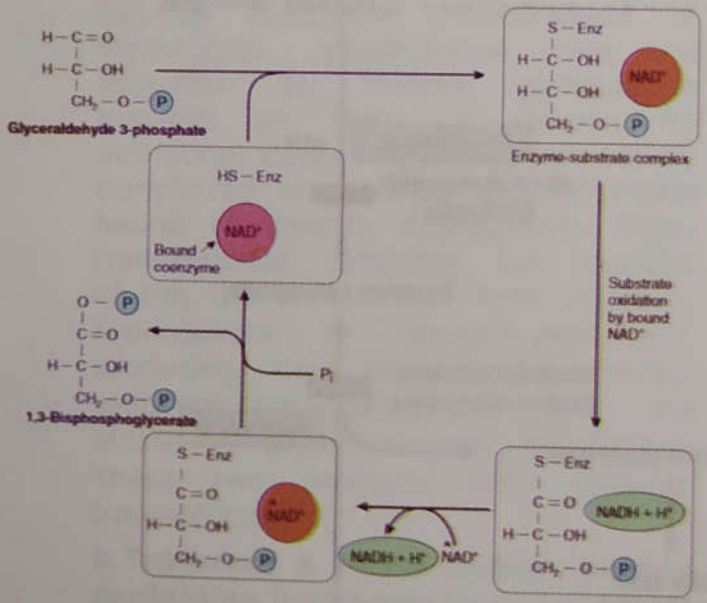
a. Enolase

b. G-6-PD

c. Phosphoglycerate Kinase-

In the reaction, catalyzed by phosphoglycerate kinase, phosphate is transferred from 1, 3- bisphosphoglycerate onto ADP, forming ATP (substrate-level phosphorylation) and 3-phosphoglycerate. Since two molecules of triose phosphate are formed per molecule of glucose undergoing glycolysis, two molecules of ATP are formed in this reaction per molecule of glucose undergoing glycolysis.

The toxicity of arsenic is the result of competition of arsenate with inorganic phosphate (Pi) in this reaction to give 1-arseno-3-phosphoglycerate, which undergoes spontaneous hydrolysis to 3-phosphoglycerate without forming ATP. 3-Phosphoglycerate is isomerized to 2-phosphoglycerate by phosphoglycerate mutase. It is likely that 2,3-bisphosphoglycerate (diphosphoglycerate, DPG) is an intermediate in this reaction.

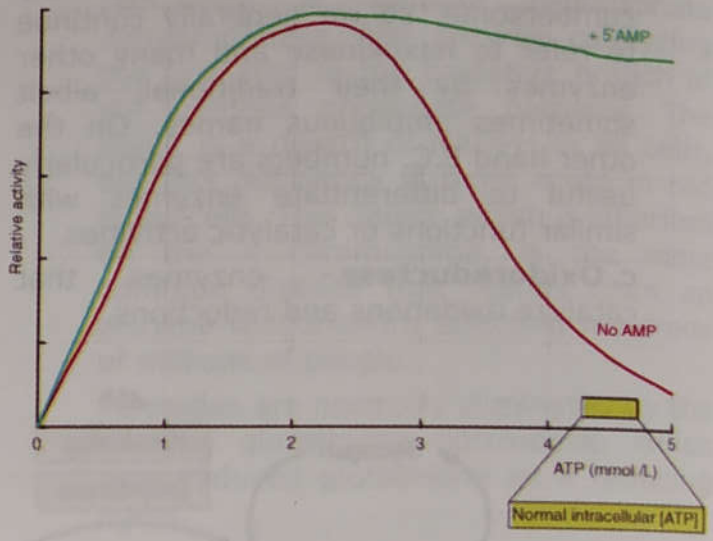


Mechanism of oxidation of glyceraldehyde 3-phosphate.(Enz, glyceraldehyde 3-phosphate dehydrogenase.)

The enzyme is inhibited by the 'SH poison iodoacetate, which is thus able to inhibit glycolysis. The NADH produced on the enzyme is not so firmly bound to the enzyme as is NAD+. Consequently, NADH is easily displaced by another molecule of NAD+.

d. Hexokinase

77. b) Citrate
d) ATP



Phosphofructokinase (phosphofructokinase-1) occupies a key position in regulating glycolysis and is also subject to feedback control. It is inhibited by citrate and by normal intracellular concentrations of ATP and is activated by 5′ AMP. At the normal intracellular [ATP] the enzyme is about 90% inhibited; this inhibition is reversed by 5′AMP .

78. b) They hold less amount of water

a. Chondroitin sulfate is a proteoglycan

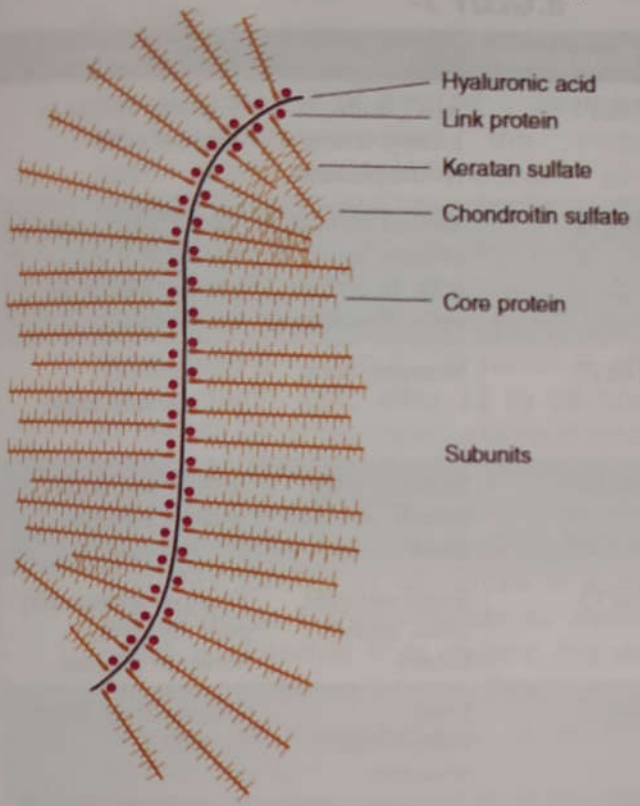
b. They hold less amount of water

c. They are made up of sugar and aminoacids

Proteoglycans & glycosaminoglycans

The Glycosaminoglycans Found in Proteoglycans Are Built Up of Repeating Disaccharides Proteoglycans are proteins that contain covalently linked glycosaminoglycans (GAGs) . At least 30 have been characterized and given names such as syndecan, betaglycan, serglycin, perlecan, aggrecan, versican, decorin, biglycan, and fibromodulin. The proteins bound covalently to glycosaminoglycans are called "core proteins." Proteoglycans vary in tissue distribution, nature of the core protein, attached glycosaminoglycans, and their function; they have proved difficult to isolate and characterize, but the use of recombinant DNA technology is beginning to yield important information about their

structures. The amount of carbohydrate in a proteoglycan is usually much greater than that found in a glycoprotein and may comprise up to 95% of its weight.



Schematic representation of the proteoglycan aggrecan: show the general structure of one particular proteoglycan, aggrecan, the major type found in cartilage. It is very large (about 2 × 103 kDa), with its overall structure resembling that of a bottlebrush.

d. They carry charge

79. d) GLUT 4

a. GLUT 1 - GLUT-1 is abundant in erythrocytes

b. GLUT 2- GLUT2, present in liver and pancreatic b cells, is distinctive in having a very high K_M value for glucose (15–20 mM). Hence, glucose enters these tissues at a biologically significant rate only when there is much glucose in the blood. The pancreas can sense the glucose level and accordingly adjust the rate of insulin secretion. The high K_M Value of GLUT2 also ensures that glucose rapidly enters liver cells only in times of plenty.

c. GLUT 3 - GLUT3, present in nearly all mammalian cells, are responsible for basal glucose uptake.

d. GLUT 4- GLUT-4 is abundant in skeletal muscle and adipose tissue.

Insulin increases the number and Promotes the activitv of GLUT-4 in skeletal muscle and adipose tissue. In type 2 diabetes mellitus, insulin resistance is observed in these tissues. This is due to the reduction in the quantity of GLUT-4 in insulin deficiency.

80. a) Glucose only

[Ref: Stryer 8th Edition]

a. Glucose only

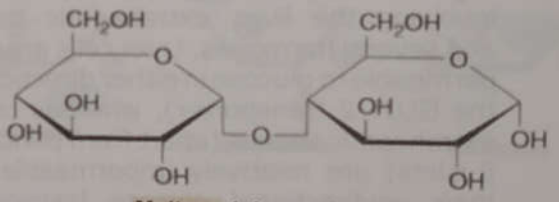
b. Fructose + glucose

c. Galactose + glucose

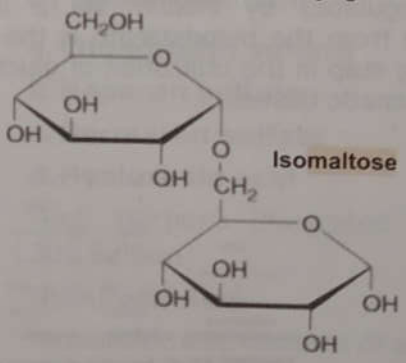
d. Galactose + fructose

Disaccharides are condensation products of two monosaccharide units, for example, lactose, maltose, isomaltose, sucrose, and trehalose.

Maltose, Sucrose, & Lactose Are Important Disaccharides The disaccharides are sugars composed of two monosaccharide residues linked by a glycoside bond .



Maltose (glucosyl-glucose)



Isomaltose

The physiologically important disaccharides are maltose, sucrose, and lactose.Hydrolysis of sucrose yields a mixture of glucose and fructose called "invert sugar" because fructose is strongly levorotatory and changes (inverts) the weaker dextrorotatory action of sucrose.

81. b) Glucosamine

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Carbohydrates Found in Glycoproteins

Hexoses	Man nose (Man), Galactose (Gal)
Acetyl hexosamines	N-Acetylglucosannine (GlcNAc), N-acetylgalactosamine (GalNAc)
Pentoses	Arabinose (Ara), Xylose (Xyl)
Methyl pentose	L-Fucose (Fuc, see Figure 15-15)
Sialic acids	N-Acyl derivatives of neuraminic acid; the predominant sialic acid is N-acetylneuraminic acid (NeuAc, see Figure 15-16)

82.

[Ref; Vasudevan 5th Edition]

a. GLUT 5-

GLUT5, present in the small intestine, functions primarily as a fructose transporter

b. GLUT 2-

The maintenance of a stable blood glucose concentration is one of the most finely regulated of all homeostatic mechanisms, involving the liver, extrahepatic tissues, and several hormones. Liver cells are freely permeable to glucose in either direction (via the GLUT 2 transporter), whereas cells of extrahepatic tissues (apart from pancreatic β-islets) are relatively impermeable, and their unidirectional glucose transporters are regulated by insulin. As a result, uptake from the bloodstream is the rate-limiting step in the utilization of glucose in extrahepatic tissues.

c. GLUT 3-

present in nearly all mammalian cells, are responsible for basal glucose uptake.

d. GLUT 7-

Transporter	Present in	Properties
GluT1	RBC, brain, kidney, colon, retina, placenta	Glucose uptake in most of cells
GluT2	Serosal surface of intestinal cells, liver, beta cells of pancreas	Low affinity; glucose uptake in liver; glucose sensor in beta cells
GluT3	Neurons, brain	High affinity; glucose into brain cells
GluT4	Skeletal, heart muscle, adipose tissue	Insulin-mediated glucose uptakev
GluT5	Small intestine, testis, sperms, kidney	Fructose transporter; poor ability to transport glucose
GluT7	Liver endoplasmic reticulum	Glucose from ERto cytoplasm
SGluT	Intestine, kidney	Cotransport; from lumen into cell

83. c) Glucose

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Fructose

b. Erythrulose

c. Glucose

Aldose-ketose isomerism:

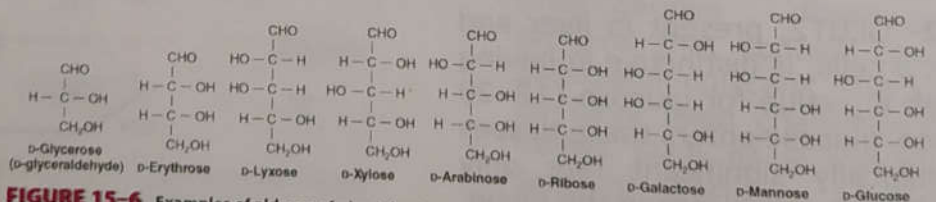


FIGURE 15–6 Examples of aldoses of physiological significance.

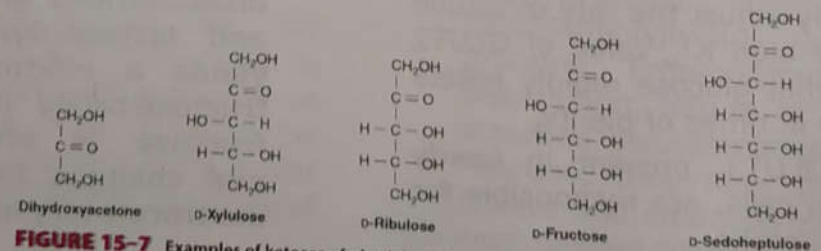


FIGURE 15–7 Examples of ketoses of physiological significance.

d. None

84. a) Liver

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Liver-

Muscle glycogen provides a readily available source of glucose-1-phosphate for glycolysis within the muscle itself. Liver glycogen functions as a reserve to maintain the blood glucose concentration in the fasting state. The liver concentration of glycogen is about 450 mmol /L glucose equivalents after a meal, falling to about 200 mmol /L after an overnight fast; after 12 to 18 hours of fasting, liver glycogen is almost totally depleted. Although muscle glycogen does not directly yield free glucose (because muscle lacks glucose-6-phosphatase), pyruvate formed by glycolysis in muscle can undergo transamination to alanine, which is exported from muscle and used for gluconeogenesis in the liver.

Storage of Carbohydrate in a 70-kg Human Being:

	Percentage of Tissue Weight	Tissue Weight	Body Content (g)
Liver glycogen	5.0	1.8 kg	90
Muscle glycogen	0.7	35kg	245
Extracellular glucose	0.1	10L	10

b. Muscle

c. Kidneys

d. Teste

85. d) beta-1-4 bond

a. Alfa 1-4 bond

b. Alfa 1-6 bond

c. beta-1-6 bond

d. beta-1-4 bond

Chitin is a structural polysaccharide in the exoskeleton of crustaceans and insects, and also in mushrooms. It consists of N-acetyl-d glucosamine units joined by $\beta 1 \rightarrow 4$ glycosidic bonds.

Pectin occurs in fruits; it is a polymer of galacturonic acid linked α-1$\rightarrow$ 4, with some galactose an/or arabinose branches, and is partially methylated

86. c) D-glucose & D-mannose

[Ref: Stryer 8th Edition]

a. D-glucose & D-fructose

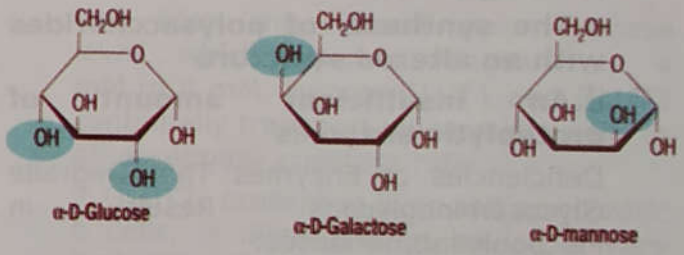
b. D-glucose & D-maltose

c. D-glucose & D-mannose

d. D-glucose & D-Aldose

e. D-galactose & D-glucose

Epimers: Isomers differing as a result of variations in configuration of the —OH and —H on carbon atoms 2, 3, and 4 of glucose are known as epimers. Biologically, the most important epimers of glucose are mannose (epimerized at carbon 2) and galactose (epimerized at carbon 4).



87. d) Hyaluronic acid

a. Chondroitin sulfate

b. Heparan sulfate

c. Dermatan sulfate

d. Hyaluronic acid

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Hyaluronic Acid

Hyaluronic acid consists of an unbranched chain of repeating disaccharide units containing GlcUA and GlcNAc. It is present in bacteria and is found in the ECM of nearly all animal tissues, but is especially high in concentration in highly hydrated types such as skin and umbilical cord, and in bone, cartilage, joints (synovial fluid) and in vitreous humor in the eye, as well as in embryonic tissues.

GAG	Sugars	Sulfate	Protein Linkage	Location
Hyaluronic acid	GlcNAc, GLcUA	-	None	Skin, synovial fluid, bone, cartilage, vitreous humor, embryonic tissues
Chondroitin sulfate	GalNAc, GlcUA	GalNAc	Xyl-Ser; associated with HA via link proteins	Cartilage, bone, CNS
Keratan sulfate I and II	GlcNAc, Gal	GlcNAc	GlcNAc-Asn (KS I) GalNAc-Thr (KS II)	Cornea, cartilage, loose connective tissue
Heparin	Gin, IdUA	GlcN GlcN IdUA	Ser	Mast cells, liver, lung, skin
Heparan sulfate	GlcN, GlcUA	GlcN	Xyl-Ser	Skin, kidney basement membrane
Dermatan sulfate	GalNAc, IdUA, (GlcUA)	GalNAc IdUA	Xyl-Ser	Skin, wide distribution

88. b) Defects in the degradation of proteoglycans

a. An increased rate of synthesis of proteoglycans

b. Defects in the degradation of proteoglycans

c. The synthesis of polysaccharides with an altered structure

d. An insufficient amount of proteolytic enzymes

Deficiencies of Enzymes That Degrade Glycosaminoglycans Result in Mucopolysaccharidoses:

Both exo- and endoglycosidases degrade GAGs. Like most other biomolecules, GAGs are subject to turnover, being both synthesized and degraded. In adult tissues, GAGs generally exhibit relatively slow turnover, their half-lives being days to weeks.

Degradation of GAGs is carried out by a battery of lysosomal hydrolases.

When GAGs are involved, these inborn errors are called mucopolysaccharidoses. None is common. In general, these conditions are chronic and progressive and affect multiple organs. Many patients exhibit organomegaly (eg, hepato- and splenomegaly; severe abnormalities in the development of cartilage and bone; abnormal facial appearance; and mental retardation. In addition, defects in hearing, vision and the cardiovascular system may be present. Diagnostic tests include analysis of GAGs in urine or tissue biopsy samples; assay of suspected defective enzymes in white blood cells, fibroblasts or serum; and test for specific genes. Prenatal diagnosis is now sometimes possible using amniotic fluid cells or chorionic villus biopsy samples. In some cases, a family history of a mucopolysaccharidosis is obtained.

89. d) Proteoglycan found in cartilage

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Meant for platelet aggregation

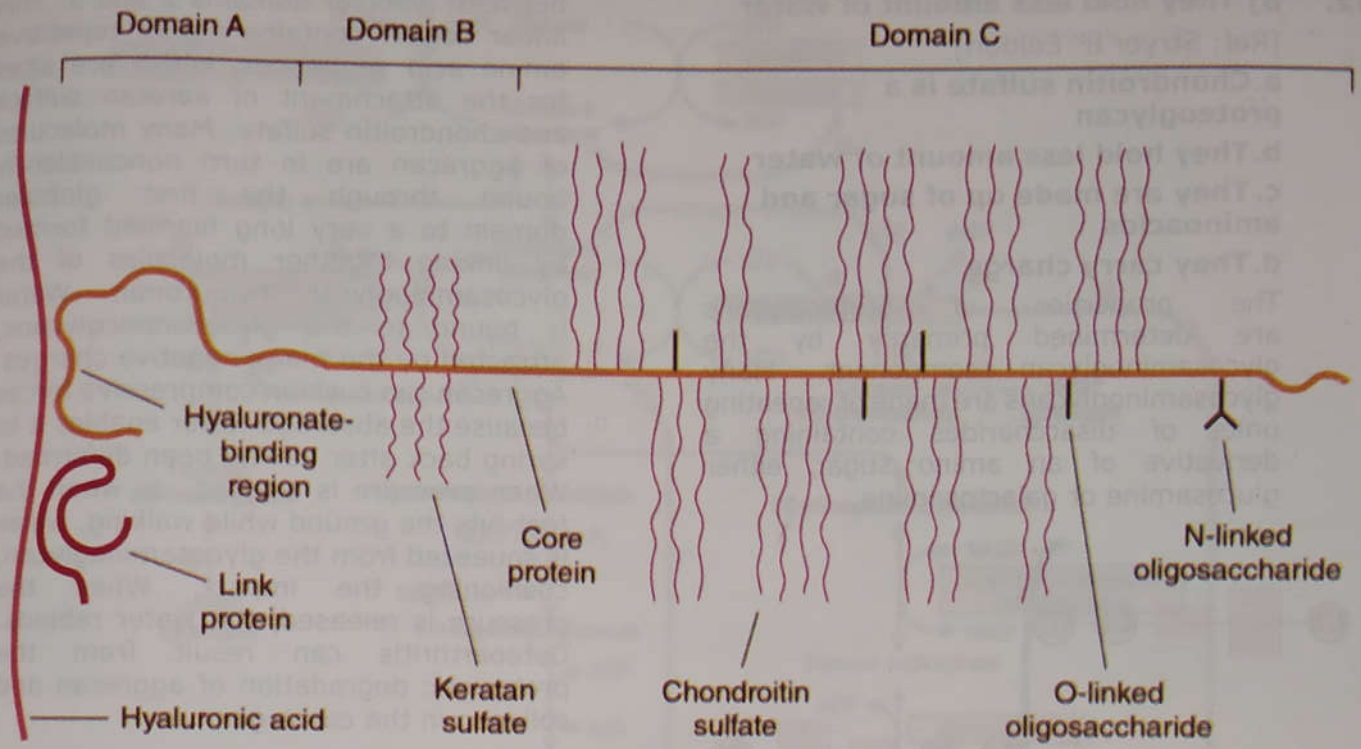
b. For adhesions of cells to basement membrane

c. For adhesion of fibrinogen receptors to plate

d. Proteoglycan found in cartilage

Aggrecan (about 2 × 103 kDa) is the major proteoglycan.

As shown it has a very complex structure, containing several GAGs (hyaluronic acid, chondroitin sulfate, and keratan sulfate) and both link and core proteins. The core protein contains three domains: A, B, and C. The hyaluronic acid binds noncovalently to domain A of the core protein as well as to the link protein, which stabilizes the hyaluronate– core protein interactions. The keratan sulfate chains are located in domain B, whereas the chondroitin sulfate chains are located in domain C; both of these types of GAGs are bound covalently to the core protein. The core protein also contains both O- and N-linked oligosaccharide chains.



Schematic diagram of the aggrecan from bovine nasal cartilage.

90. b) Sodium citrate

a. Heparin

b. Sodium citrate

c. Double oxalate

d. Na

91. c) Adipocytes

[Ref: Stryer 8th Edition]

a. Brain cells

b. Heatocytes

c. Adipocytes

Several glucose transporters mediate the thermodynamically downhill movement of glucose across the plasma membranes of animal cells. Each member of this protein family, named GLUT1 to GLUT5, consists of a single polypeptide chain about 500 residues long . Each glucose transporter has a 12-transmembrane-helix structure similar to that of lactose permease.

The members of this family have distinctive roles:

1. GLUT1 and GLUT3, present in nearly all mammalian cells, are responsible for basal glucose uptake. Their KM value for glucose is about 1 mM, significantly less than the normal serum-glucose level, which typically ranges from 4 mM to 8 mM. Hence, GLUT1 and GLUT3 continually transport glucose into cells at an essentially constant rate.

2. GLUT2, present in liver and pancreatic b cells, is distinctive in having a very high KM value for glucose (15–20 mM). Hence, glucose enters these tissues at a biologically significant rate only when there is much glucose in the blood. The pancreas can sense the glucose level and accordingly adjust the rate of insulin secretion. The high KM value of GLUT2 also ensures that glucose rapidly enters liver cells only in times of plenty.

3. GLUT4, which has a KM value of 5 mM, transports glucose into muscle and fat cells. The number of GLUT4 transporters in the plasma membrane increases rapidly in the presence of insulin, which signals the fed state. Hence, insulin promotes the uptake of glucose by muscle and fat. Endurance exercise training increases the amount of this transporter present in muscle membranes.

4. GLUT5, present in the small intestine, functions primarily as a fructose transporter.

d. RBCs

92. b) They hold less amount of water

[Ref: Stryer 8th Edition]

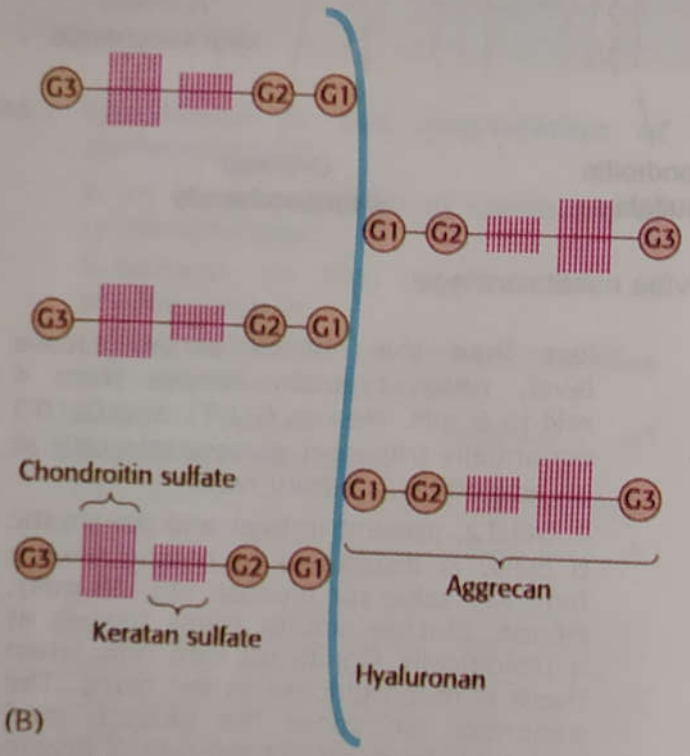
a. Chondroitin sulfate is a proteoglycan

b. They hold less amount of water

c. They are made up of sugar and aminoacids

d. They carry charge

The properties of proteoglycans are determined primarily by the glycosaminoglycan component. Many glycosaminoglycans are made of repeating units of disaccharides containing a derivative of an amino sugar, either glucosamine or galactosamine.



(B)

Among the best-characterized members of this diverse class is the proteoglycan in the extracellular matrix of cartilage. The proteoglycan aggrecan and the protein collagen are key components of cartilage. The triple helix of collagen provides structure and tensile strength, whereas aggrecan serves as a shock absorber. The protein component of aggrecan is a large molecule composed of 2397 amino acids. The protein has three globular domains, and the site of glycosaminoglycan attachment is the extended region between globular domains 2 and 3. This linear region contains highly repetitive amino acid sequences, which are sites for the attachment of keratan sulfate and chondroitin sulfate. Many molecules of aggrecan are in turn noncovalently bound through the first globular domain to a very long filament formed by linking together molecules of the glycosaminoglycan hyaluronan .Water is bound to the glycosaminoglycans, attracted by the many negative charges. Aggrecan can cushion compressive forces because the absorbed water enables it to spring back after having been deformed. When pressure is exerted, as when the foot hits the ground while walking, water is squeezed from the glycosaminoglycan, cushioning the impact. When the pressure is released, the water rebinds. Osteoarthritis can result from the proteolytic degradation of aggrecan and collagen in the cartilage.

93. c) Galactosemia

a. Fanconi anmia

b. Lactose intolerance

c. Galactosemia

d. Phenylketonuria

e. Salicylate poisoning

Glucose is a reducing sugar:

Because the alpa and beta isomers of glucose are in an equilibrium that passes through the open-chain form, glucose has some of the chemical properties of free aldehydes, such as the ability to react with oxidizing agents. For example, glucose can react with cupric ion (Cu^{2+}), reducing it to cuprous ion (Cu+), while being oxidized to gluconic acid.

94. c) Phosphoglucomutase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

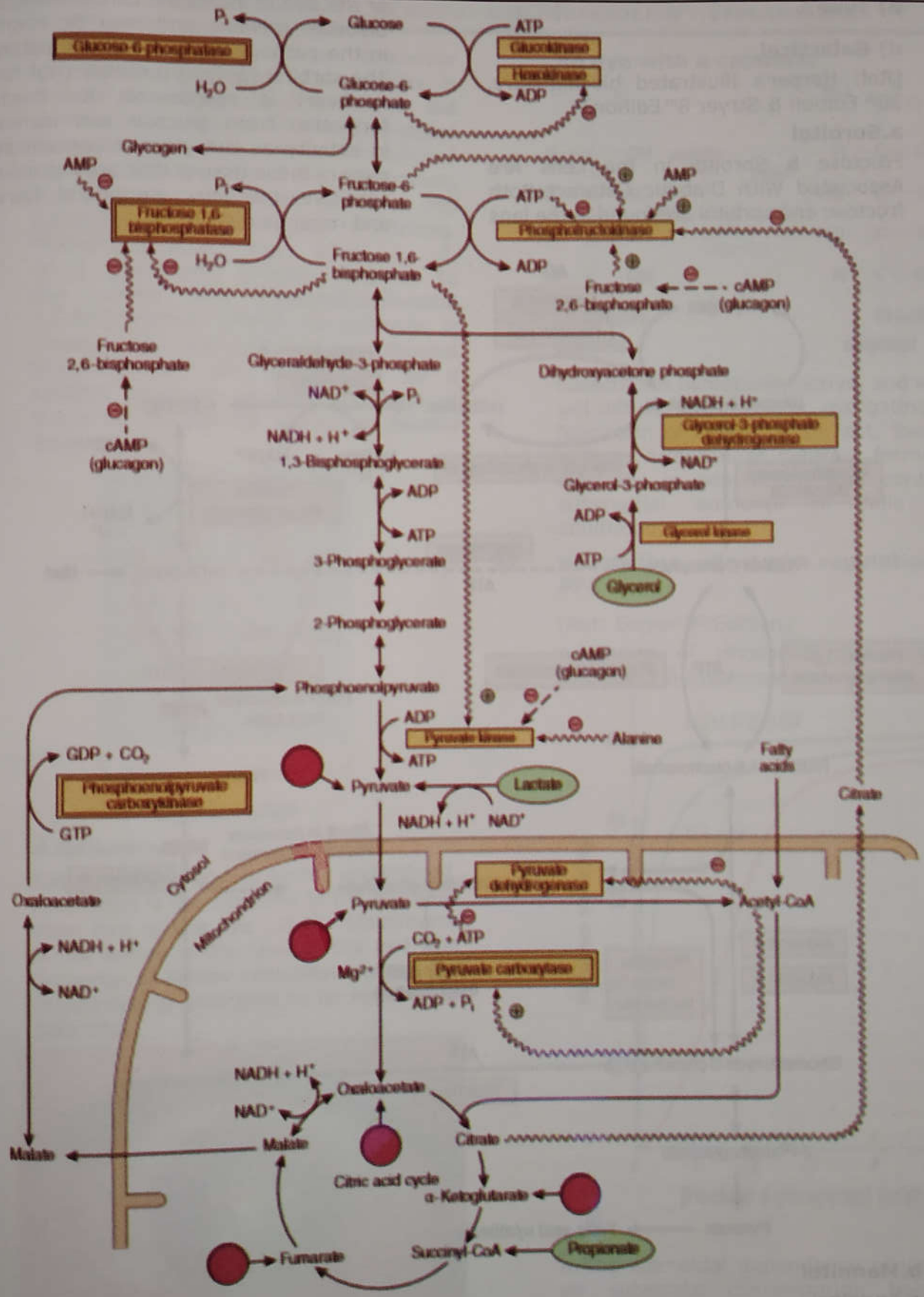
a. Phosphoglycerate kinase

b. Fructose 1,6 biphosphatese

c. Phosphoglucomutase

d. Pyruvate carboxylase

e. Isomerase



Major pathways and regulation of gluconeogenesis and glycolysis in the liver.

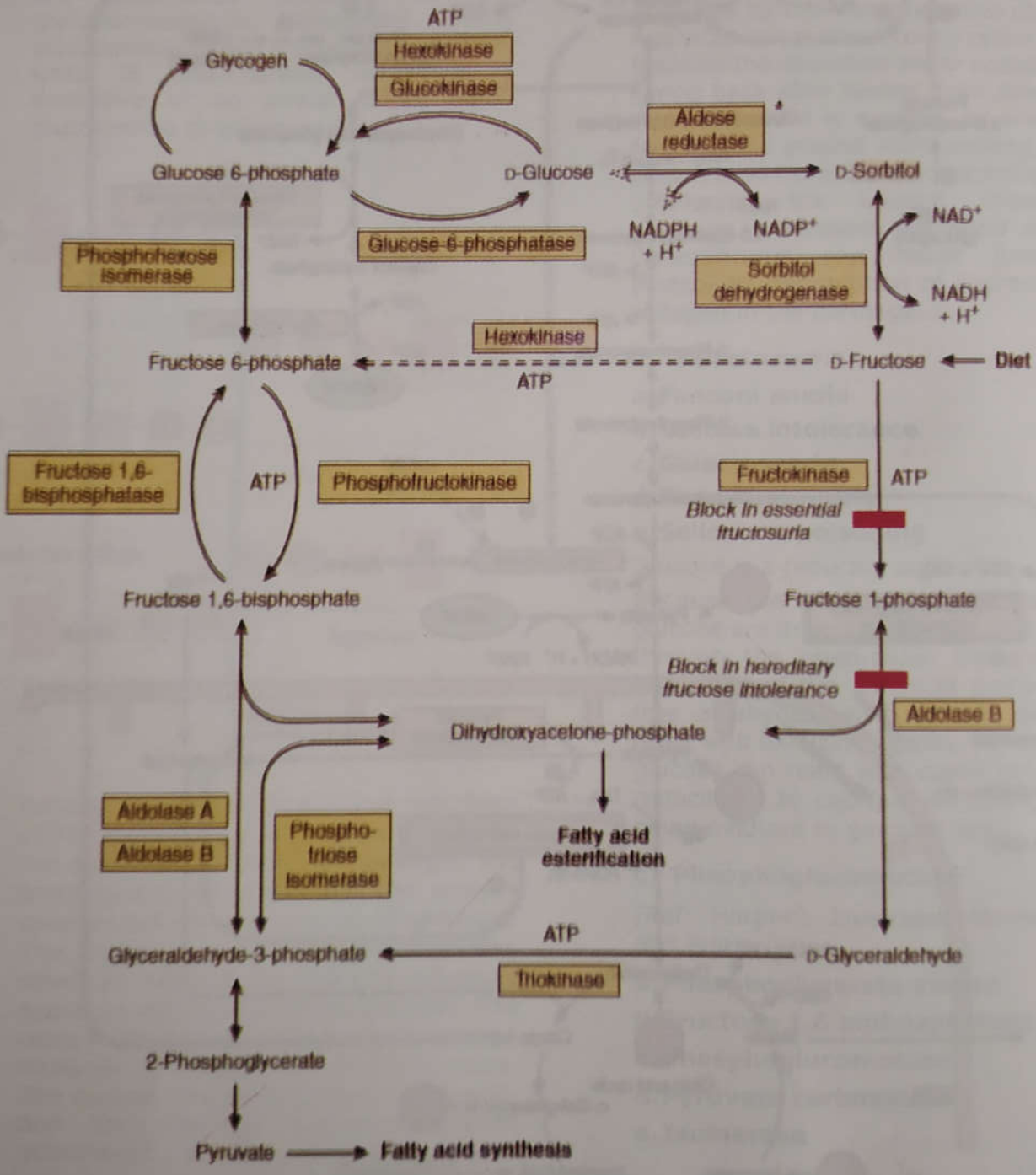
95. a) Type I

96. d) Galacticol

[Ref: Harper's Illustrated biochemistry, 30th Edition & Stryer 8th Edition]

a. Sorbitol

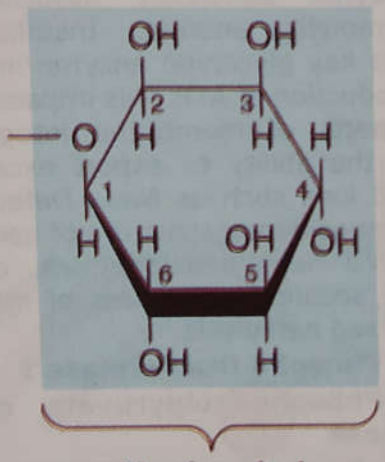
Fructose & Sorbitol in the Lens Are Associated With Diabetic Cataract Both fructose and sorbitol are found in the lens of the eye in increased concentrations in diabetes mellitus and may be involved in the pathogenesis of diabetic cataract. The sorbitol (polyol) pathway (not found in liver) is responsible for fructose formation from glucose and increases in activity as the glucose concentration rises in those tissues that are not insulin-sensitive—the lens, peripheral nerves, and renal glomeruli.



b. Mannitol

c. Inositol

Phosphatidylinositol Is a Precursor of Second Messengers The inositol is present in phosphatidylinositol as the stereoisomer, myoinositol. Phosphorylated phosphatidylinositols (phosphoinositides) are minor components of cell membranes, but play an important part in cell signaling and membrane trafficking. Phosphoinositides may have 1, 2, or 3 phosphate groups attached to the inositol ring. Phosphatidylinositol 4,5-bisphosphate (PiP2), for example, is cleaved into diacylglycerol and inositol tris-phosphate upon stimulation by a suitable hormone agonist, and both of these act as internal signals or second messengers.

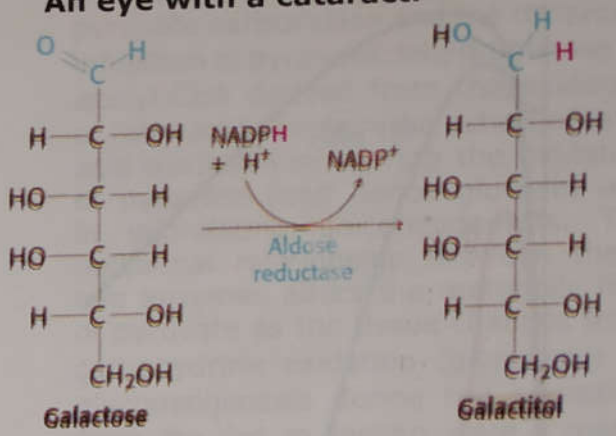


Myoinositol

d. Galacticol

Cataract formation is better understood. A cataract is the clouding of the normally clear lens of the eye . If the transferase is not active in the lens of the eye, the presence of aldose reductase causes the accumulating galactose to be reduced to galactitol.

An eye with a cataract.

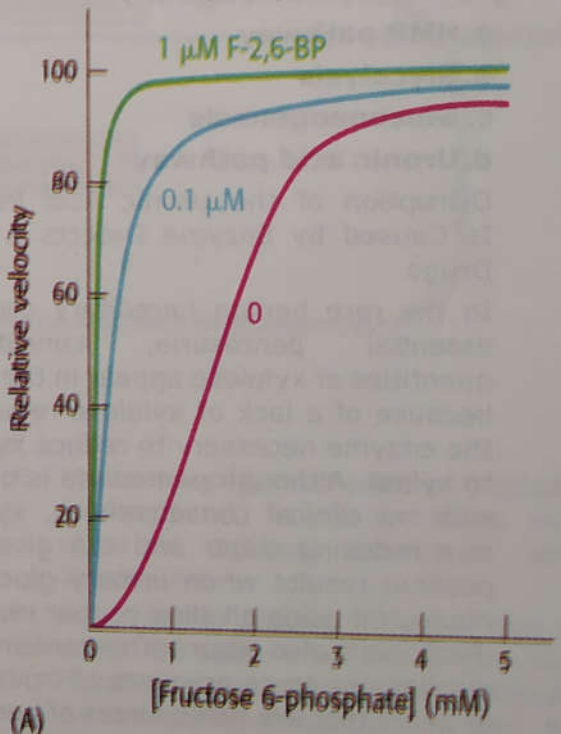


Galactitol is osmotically active, and water will diffuse into the lens, instigating the formation of cataracts. In fact, there is a high incidence of cataract formation with age in populations that consume substantial amounts of milk into adulthood.

97. b) Positive allosteric regulation of PFK-1

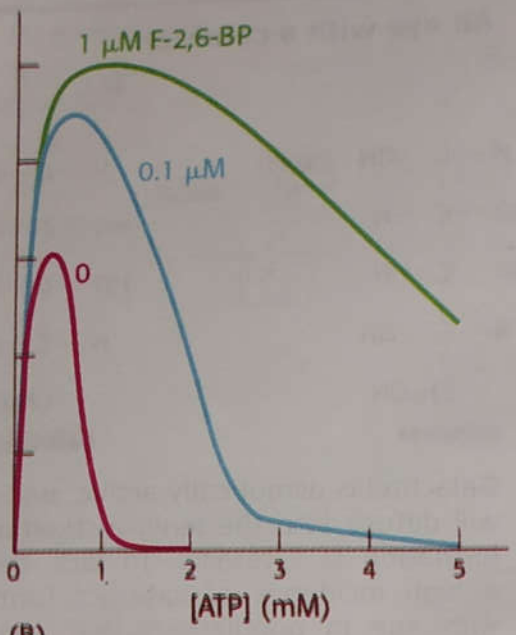
[Ref: Stryer 8th Edition]

Activation of phosphofructokinase by fructose 2,6-bisphosphate.



(A)

a. The sigmoidal dependence of velocity on substrate concentration becomes hyperbolic in the presence of 1 mM fructose 2,6-bisphosphate.



(B)

b. ATP, acting as a substrate, initially stimulates the reaction. As the concentration of ATP increases, it acts as an allosteric inhibitor. The inhibitory effect of ATP is reversed by fructose 2,6-bisphosphate.

98. d) Uronic acid pathway

a. HMP pathway

b. Glycolysis

c. Gluconeogenesis

d. Uronic acid pathway

Disruption of the Uronic Acid Pathway Is Caused by Enzyme Defects & Some Drugs

In the rare benign hereditary condition essential pentosuria, considerable quantities of xylulose appear in the urine, because of a lack of xylulose reductase, the enzyme necessary to reduce xylulose to xylitol. Although pentosuria is benign, with no clinical consequences, xylulose is a reducing sugar and can give false positive results when urinary glucose is measured using alkaline copper reagents .Pentosuria also occurs after consumption of relatively large amounts of fruits such as pears that are rich sources of pentoses (alimentary pentosuria).

99. a) Pyruvate kinase

[Ref: Stryer 8th Edition]

a. Pyruvate kinase

Pyruvate kinase (PK) deficiencya (OMIM 266200) -A variety of mutations in the gene for the R (red cell) isozyme of PK Inherited aldolase A deficiency and pyruvate kinase deficiency in erythrocytes cause hemolytic anemia. The exercise capacity of patients with muscle phosphofructokinase deficiency is low, particularly if they are on high-carbohydrate diets. By providing lipid as an alternative fuel, for example, during starvation, when blood free fatty acid and ketone bodies are increased, work capacity is improved. Deficiency of pyruvate kinase is the second most common, albeit infrequent, enzyme deficiency associated with hemolytic anemia. Insufficiency of this key glycolytic enzyme impairs the production of ATP. This impacts multiple aspects of membrane integrity such as the ability to export excess water and ions such as Na+. Defects in the composition or structure of hemoglobin, called hemoglobinopathies, constitute the second major class of intrinsically caused hemolysis.

b. Phospho fructokinase I

c. Phosphoenolpyruvate carboxy-kinase

d. glucose 6- phosphatase

100. b) Lysosomes

[Ref: Lippincott's illustrated reviews, 6th Edition]

a. Golgi apparatus

b. Lysosomes

I-cell disease Deficiency of GlcNAc phosphotransferase, resulting in abnormal targeting of certain lysosomal enzymes.Inclusion Cell (I-Cell) Disease Results from Faulty Targeting of Lysosomal Enzymes Mannose 6-phosphate serves to target enzymes into the lysosome.

c. Peroxisomes

d. Mitochondria

101. d) Acetyl CoA

a. Succinate

b. AMP

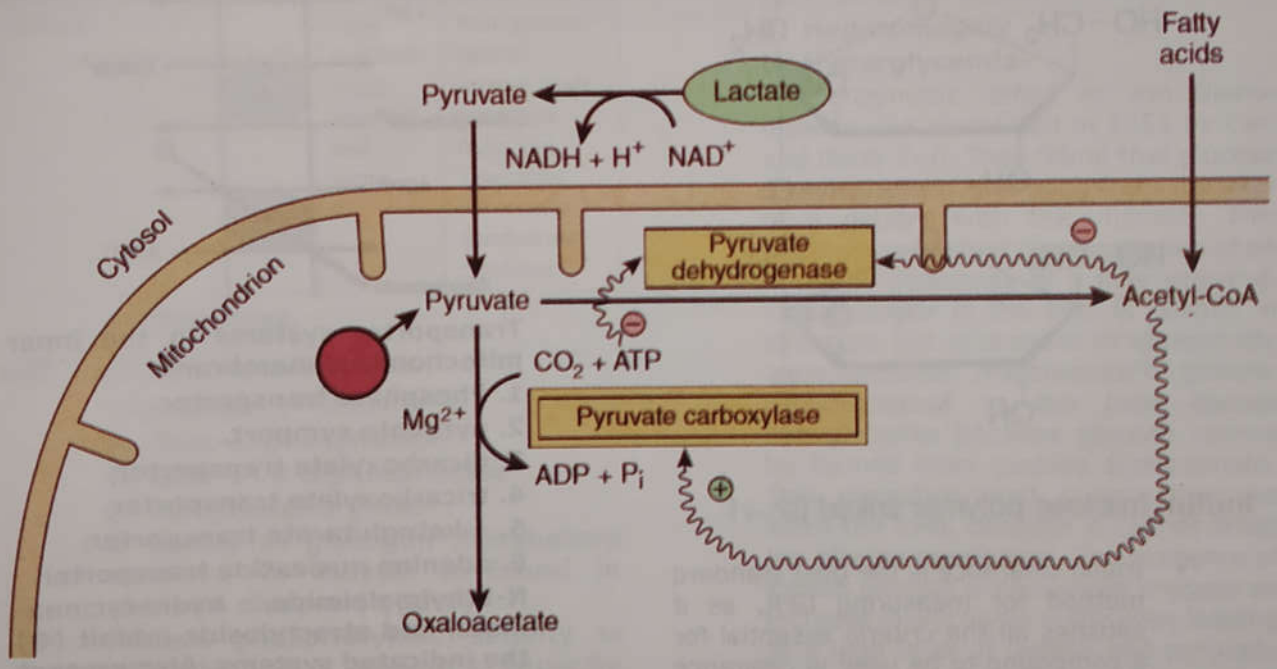
c. Isocitrate

d. Acetyl CoA

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Allosteric Modification Is Instantaneous

In gluconeogenesis, pyruvate carboxylase, which catalyzes the synthesis of oxaloacetate from pyruvate, requires acetyl-CoA as an allosteric activator. The addition of acetyl-CoA results in a change in the tertiary structure of the protein, lowering the Km for bicarbonate. This means that as acetyl-CoA is formed from pyruvate, it automatically ensures the provision of oxaloacetate and, therefore, its further oxidation in the citric acid cycle, by activating pyruvate carboxylase. The activation of pyruvate carboxylase and the reciprocal inhibition of pyruvate dehydrogenase by acetyl-CoA derived from the oxidation of fatty acids explain the action of fatty acid oxidation in sparing the oxidation of pyruvate (and hence glucose) and in stimulating gluconeogenesis. The reciprocal relationship between these two enzymes alters the metabolic fate of pyruvate as the tissue changes from carbohydrate oxidation (glycolysis) to gluconeogenesis during the transition from the fed to fasting state.A major role of fatty acid oxidation in promoting gluconeogenesis is to supply the ATP that is required.



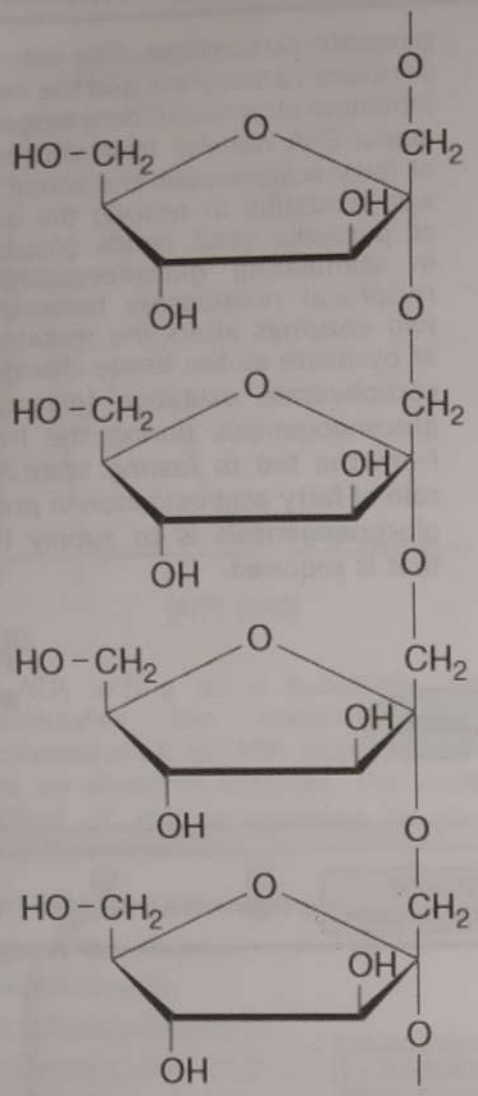
102. b) Beta configuration of of anomeic C_2

[Ref: Stryer 8th Edition]

a. Absence of digestive enzyme in the upper GIT

b. Beta configuration of of anomeic C_2

- inulin, the storage carbohydrate in some plants
- Inulin is a polysaccharide of fructose (a fructosan) found in tubers and roots of dahlias, artichokes, and dandelions.
- It is readily soluble in water and is used to determine the glomerular filtration rate but it is not hydrolyzed by intestinal enzymes, so has no nutritional value.



Inulin: fructose polymer linked β2→1

- Inulin clearance is the gold standard method for measuring GFR, as it satisfies all the criteria essential for a compound to be used in clearance tests. However, unlike creatinine, inulin is an exogenous compound that has to be infused intravenously at a constant rate.

c. Low pH of the stomach

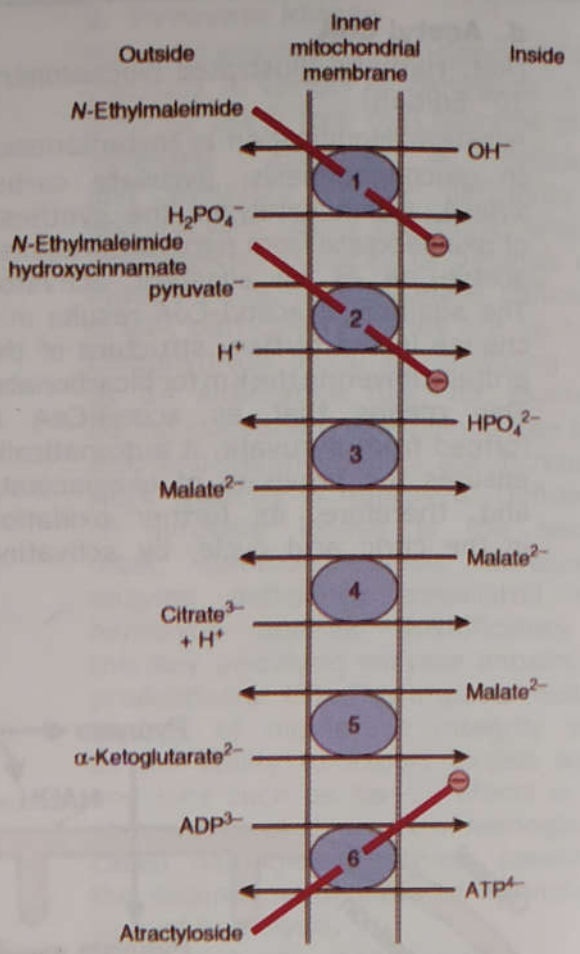
d. Presence of α –Glycosidic linkages

103. b) Proton symport

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Chloride antiport

b. Proton symport



Transporter systems in the inner mitochondrial membrane.
1. Phosphate transporter,
2. pyruvate symport,
3. dicarboxylate transporter,
4. tricarboxylate transporter,
5. α-ketoglutarate transporter,
6. adenine nucleotide transporter.
N-Ethylmaleimide, hydroxycinnamate, and atractyloside inhibit (⊖) the indicated systems. Also present (but not shown) are transporter systems for glutamate/aspartate ,glutamine, ornithine, neutral amino acids, and carnitine.

c. ATP dependent antiport

d. Facilitated uniport

104. c) Sucrose

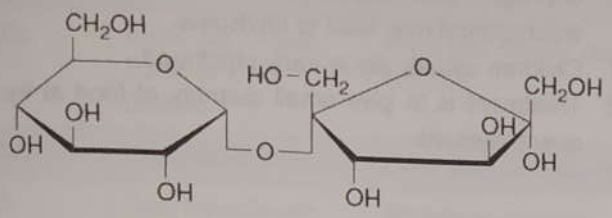
[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Fructose

b. Maltose

c. Sucrose

Hydrolysis of sucrose yields a mixture of glucose and fructose called "invert sugar" because fructose is strongly levorotatory and changes (inverts) the weaker dextrorotatory action of sucrose.



Sucrose (glucosyl-fructose)

Sugar	Composition	Source	Clinical Significance
Sucrose	0-a-D-glucopyranosyl-(1→2)-β-$_D$-fructofuranoside	Cane and beet sugar, sorghum and some	Rare genetic lack of sucrase leads to sucrose fruits and vegetables intolerance—diarrhea and flatulence

d. Galactose

105. c) Myophosphorylase

[Ref: Stryer 8th Edition]

a. Gluc-1, phosphatase

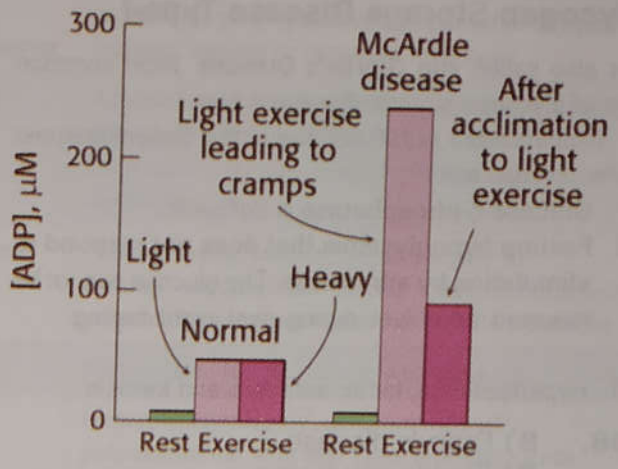
b. Gluc-1 , 6 diphosphatase

c. Myophosphorylase-

A defect in glycogen metabolism confined to muscle is found in McArdle disease (type V):

Muscle phosphorylase activity is absent, and a patient's capacity to perform strenuous exercise is limited because of painful muscle cramps. The patient is otherwise normal and well developed. Thus, effective utilization of muscle glycogen is not essential for life.

NMR study of human arm muscle. The level of ADP during exercise increases much more in a patient with McArdle glycogen-storage disease (type V) than in normal controls.



d. hepatic phosphorylation

106. b) Hyperglycemia

[Ref: Stryer 8th Edition]

a. Hepatomegaly

b. Hyperglycemia-

The enzymatic defect in von Gierke disease was elucidated in 1952 by Carl and Gerty Cori. They found that glucose 6-phosphatase is missing from the liver of a patient with this disease. This finding was the first demonstration of an inherited deficiency of a liver enzyme. The glycogen in the liver is normal in structure but is present in abnormally large amounts. The absence of glucose 6-phosphatase in the liver causes hypoglycemia because glucose cannot be formed from glucose 6-phosphate. This phosphorylated sugar does not leave the liver, because it cannot cross the plasma membrane. The presence of excess glucose 6-phosphate triggers an increase in glycolysis in the liver, leading to a high level of lactate and pyruvate in the blood. Patients who have von Gierke disease also have an increased dependence on fat metabolism. This disease can also be produced by a mutation in the gene that encodes the glucose 6-phosphate transporter.

c. Lactic aciodosis

d. Hyperlipidemia

107. a) I

[Ref; Vasudevan 5th Edition]

Glycogen Storage Disease Type-I

It is also called **von Gierke's Disease**. Most common type of glycogen storage disease is type I.

Incidence is 1 in 100,000 live births. Salient features of the disease are:

1. **Glucose-6-phosphatase** is deficient.
2. **Fasting hypoglycemia that does not respond to stimulation by adrenaline**. The glucose cannot be released from liver during over night fasting
3. Hyperlipidemia, **lactic acidosis** and **ketosis**.
4. Glucose-6-phosphate is accumulated, so it is channeled to HMP shunt pathway (described below) producing more ribose and more purine nucleotides.
5. Purines are then catabolized to uric acid, leading to **hyperuricemia**
6. Glycogen gets deposited in liver. Massive liver enlargement may lead to **cirrhosis**.
7. Children usually die in early childhood.
8. Treatment is to give small quantity of food at frequent intervals.

108. **B)** Fabry's disease
D) Fragile syndrome
E) Krabbe's disease

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Type	Name	Enzyme Deficiency	Clinical Features
0	—	Glycogen synthase	Hypoglycemia; hyperketonemia; early death
Ia	Von Gierke disease	Glucose-6-phosphatase	Glycogen accumulation in liver and renal tubule cells; hypoglycemia; lactic acidemia; ketosis; hyperlipemia
Ib	—	Endoplasmic reticulum glucose-6- phosphate transporter	As type Ia; neutropenia and Impaired neutrophil function leading to recurrent infections
II	Pompe disease	Lysosomal $a_1 \rightarrow 4$ and $a_1 \rightarrow 6$ glucosidase (acid maltase)	Accumulation of glycogen in lysosomes: juvenile onset variant, muscle hypotonia, death from heart failure by age 2; adult onset variant, muscle dystrophy
IIIa	Limit dextrinosls, Forbe or Corl disease	Liver and muscle debranching enzyme	Fasting hypoglycemia; hepatomegaly In Infancy; accumulation of characteristic branched polysaccharide (limit dextrin); muscle weakness
IIIb	Limit dextrinosls	Liver debranching enzyme	As type Ilia, but no muscle weakness
IV	Amylopectlnosis, Andersen disease	Branching enzyme	Hepatosplenomegaly; accumulation of polysaccharide with few branch points; death from heart or liver failure before age 5
V	Myophosphorylase deficiency, McArdle syndrome	Muscle phosphorylase	Poor exercise tolerance; muscle glycogen abnormally high (2.5%-4%); blood lactate very low after exercise
VI	Hers disease	Liver phosphorylase	Hepatomegaly; accumulation of glycogen In liver; mild hypoglycemia; generally good prognosis

109. **b) Debranching enzyme**

Type	Name	Enzyme Deficiency	Clinical Features
0	—	Glycogen synthase	Hypoglycemia; hyperketonemia; early death
Ia	Von Gierke disease	Glucose-6-phosphatase	Glycogen accumulation in liver and renal tubule cells; hypoglycemia; lactic acidemia; ketosis; hyperlipemia

Ib	—	Endoplasmic reticulum glucose-6- phosphate transporter	As type Ia; neutropenia and Impaired neutrophil function leading to recurrent infections
II	Pompe disease	Lysosomal $a_1 \rightarrow 4$ and $a_1 \rightarrow 6$ glucosidase (acid maltase)	Accumulation of glycogen in lysosomes: juvenile onset variant, muscle hypotonia, death from heart failure by age 2; adult onset variant, muscle dystrophy
IIIa	Limit dextrinosls, Forbe or Corl disease	Liver and muscle debranching enzyme	Fasting hypoglycemia; hepatomegaly In Infancy; accumulation of characteristic branched polysaccharide (limit dextrin); muscle weakness
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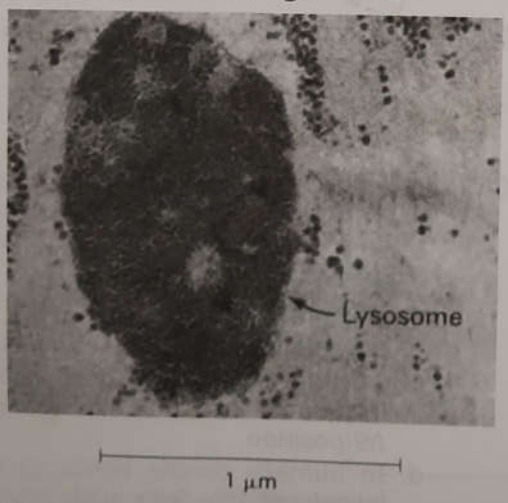
V	Myophosphorylase deficiency, McArdle syndrome	Muscle phosphorylase	Poor exercise tolerance; muscle glycogen abnormally high (2.5%-4%); blood lactate very low after exercise
VI	Hers disease	Liver phosphorylase	Hepatomegaly; accumulation of glycogen In liver; mild hypoglycemia; generally good prognosis

110. c) Von Gierke disease

111. c) Acid maltase deficiency

[Ref: Stryer 8th Edition]

In Pompe disease (type II), lysosomes become engorged with glycogen because they lack a-1,4-glucosidase, a hydrolytic enzyme confined to these organelles :



Glycogen-engorged lysosome.

This electron micrograph shows skeletal muscle from an infant with type II glycogen-storage disease (Pompe disease). The lysosomes are filled with glycogen because of a deficiency in a-1,4-glucosidase, a hydrolytic enzyme confined to lysosomes. The amount of glycogen in the cytoplasm is normal.

e. Tay Sachs disease

112. b) McArdle's disease
d) Pompe's disease

[Ref: Lippincott's illustrated reviews, 6th Edition]

AN EXTRA MILE:

For Pompe's Disease:

Enzyme replacement therapy is now available for treatment of infantile-onset Pompe's disease. The enzyme designated as Myozyme (recombinant human acid alpha glucosidase, rhGAA) is administered intravenously and is approved in US by FDA.The drug is very expensive currently and has to be taken life-long.

Lipids – Questions

Q1. True about role of phospholipids:

a. Cell to cell recognition
b. Cell signaling
c. Precursor of Second Messengers
d. Mediators of inflammation
e. Regulate membrane permeability

Q2. Correct statement about membrane:

a. Phospholipids undergo rapid lateral diffusion
b. Transverse movement of lipids across the membrane is faster than protein
c. Hydrophobic core of the phospholipid bilayer remains constantly in motion because of rotations around the bonds of lipid tails
d. Phospholipids that have one fatty acyl group, cannot form the bilayer
e. Phospholipids span whole bilayer

Q3. The amino acid sequence of Lipoprotein A is homologous to which of the following proteins?

a. Plasminogen b. Albumin
c. Prothrombin d. Plasmin

Q4. Enzyme which is active in well fed state is:

a. Carnitine palmitoy1 transferase 1
b. Pyruvate carboxylase
c. Acetyl CoA carboxylase
d. HMG lyase

Q5. Which of the following enzymes is necessary for extrahepatic utilisation of ketone bodies?

a. Thiophorase
b. HMGCoA lyase
c. HMG-CoA reductase
d. Succinate dehydrogenase

Q6. Enzyme required for synthesis of both ketone bodies and cholesterol is:

a. HMG CoA reductase
b. HMG CoA synthase
c. Acetyl CoA carboxylase
d. HMG CoA lyase

Q7. Catabolism of long chain fatty acids occur in:

a. Mitochondria b. Peroxisome
c. Endolysosome d. Golgi bodies

Q8. Endoplasmic reticulum is a site for _____.

a. Glycolysis
b. Triacylglycerol synthesis
c. Protein synthesis
d. Protein packaging

Q9. A deficiency of carnitine might be expected to interfere with:

a. β-oxidation.
b. Ketone body formation from acetyl CoA.
c. Palmitate synthesis.
d. Mobilization of stored triacylglycerols from adipose tissue.

Q10. Lipotropic factors are all except?

a. Choline b. Lecithine
c. Arginine d. Methionine

Q11. Amino acid used in Carnitine synthesis is?

a. Alanine b. Lysine
c. Arginine d. Tyrosine

Q12. Menadione is an analogue of α-Linolenic acid is considered to be nutritionally essential in humans BECAUSE:

a. It is an ω3 fatty acid.
b. It contains three double bonds.
c. In humans double bonds cannot be introduced into fatty acids beyond the Δ9 position.
d. In humans double bonds cannot be introduced into fatty acids beyond the Δ12 position.

1. b, c, d, e,	2. a, c, d	3. a	4. c	5. a	6. b	7. a
8. b	9. a	10. c	11. b	12. c		

Q13. I cell disease is associated with:
a. Golgi apparatus b. Lysosomes
c. Peroxisomes d. Mitochondria

Q14. ATP yield in stearic acid oxidation:
a. 146 ATP b. 120ATP
c. 129 ATP d. 139 ATP

Q15. Which one of the following tissues can metabolize glucose, fatty acids, and ketone bodies for ATP production?
a. RBC-- b. Muscle
c. Hepatocytes d. Brain

Q16. Which of the following is the defect in type 2 familial hypercholesterolemia?
a. Absence of VLDL receptor
b. Absence of hepatic LDL receptor
c. Defective apoE
d. Over production of VLDL

Q17. True about mucopolysacchardoses:
a. It is a type of lysosomal storage disorder
b. All are autosomal recessive except Morquio syndrome
c. Skeletal defect is manifested as dystosis multiplex
d. Research is going on to develop give therapy for Morquio syndrome

Q18. Which of the following are omega-6 fatty acid except:
a. Palmitic acid
b. Alpha-linolenic acid
c. Linoleic acid
d. Gamma linolenic acid
e. Arachidonic acid

Q19. Apolipoproteins present in HDL cholesterol is/are:
a. Apo A I b. Apo A II
c. Apo B-48 d. Apo 100
e. Apo D

Q20. Both triglycerides and HDL are increased by:
a. Smoking
b. Athletes
c. Statin and anabolic steroid abusers
d. Alcoholism

Q21. Apo-48 is apolipoprotein specific for:
a. Chylomicron b. LDL
c. VLDL d. HDL

Q22. Emulsification of lipids in the small intestine
a. Pancreatic lipase
b. Gastric lipase
c. Bile salts
d. Bile pigments

Q23. Allosteric activator of Acetyl CoA carboxylase
a. Malonyl CoA b. Acetyl CoA
c. Citrate d. Biotin

Q24. Beta-oxidation of odd-chain fatty acids produces
a. Succinyl CoA b. Propionyl CoA
c. Acetyl CoA d. Malonyl CoA

Q25. Cholesterol is transported to extrahepatic tissue mainly through
a. VLDL b. LDL
c. Chylomicrons d. HDL
e. All of the above

Q26. Which of the following is required for fatty acid synthesis?
a. NADPH b. NADH
c. FADH d. None

Q27. Apoprotein-C
a. Activates lipoprotein lipase
b. Inactivates lipoprotein lipase
c. Facilitates triglyceride transport
d. All of the above

Q28. In Zellweger syndrome, there is
a. Accumulation of long fatty acids
b. Accumulation of short chain fatty acids
c. Accumulation of very long chain fatty acids
d. Accumulation of medium chain fatty acids

Q29. Ketone bodies are by products of metabolism of
a. Carbohyrate b. Protein
c. Fat d. All of the above

13. b	14. b	15. b	16. b	17. a, c, d	18. a, b	19. a, b, e	20. d	21. a
22. e	23. c	24. b	25. b	26. a	27. b	28. c	29. c	

Q30. The daily normal excretion of Ketone bodies is

a. 0.1 mg b. 0.5 mg
c. 1.0mg d. 2.0 mg

Q31. Which of the following is seen in obstructive jaundice?

a. Excess of urobilinogen in urine
b. Excess of unconjugated serum bilirbin
c. Excess of bile salts in the urine
d. All of the above

Q32. Hypolipidemic agents act on

a. HMG CoA synthetase
b. HMG CoA oxygenase
c. HMG CoA reductase
d. HMG CoA hydratase
e. HMGCoAmutase

Q33. Which is not encountered in HMG CoA pathway?

a. Cholesterol b. Mevalonate
c. Acetyl Co A d. Pyruvate

Q34. Which of the following is a product of microbial reduction?

a. Cholic acid b. Glycine
c. Coprostanol d. Pregnenolone

Q35. Arachidonic acid is a precursor of

a. Prostaglandin and lipase
b. Lipase steroid and leukotriene
c. Lipase and leukotriene
d. Leukotriene and prostaglandin

Q36. "Squalene" is the intermediate product during synthesis of

a. VLDL b. Cholesterol
c. Tachysterol d. Lanosterol

Q37. A fatty acid not synthesized in man is

a. Palmitoleic acid b. Linoleic acid
c. Oleic acid d. Palmitic acid
e. Stearic acid

Q38. The rate limiting step in the extra mitochondrial synthesis of fatty acids is

a. Condensing enzyme
b. Acetyl CoA enzyme
c. Acetyl Transferase
d. Palmitoyl Deacylase

Q39. Cholesterol contains

a. 27 carbon atoms
b. 4 rings
c. A hydroxyl group of carbon number 4
d. A double bond between carbon number 15 and carbon number 16

Q40. The regulatory enzyme for cholesterol biosynthesis is

a. HMG CoA synthase
b. HMG CoA reductase
c. Acetyl CoA carboxylase
d. Mevalonate synthase

Q41. All are active against hormone Sensitive lipase

a. Adrenaline b. Insulin
c. Norepinephrine d. Nicotinicacid

Q42. The enzyme LCAT (Lecithine Cholesterol Acyl Transferase)

a. Is involved in the formation of chylomicrons
b. Hydrolyses triglyceride into glycerol and fatty acids
c. Helps in the conversion of cholesterol ester
d. Is one of the enzymes involved in cholesterol biosynthesis

Q43. Which of the following is a cardioprotective fatty acid?

a. Palmitic acid
b. Stearic acid
c. Oleic acid
d. Omega3 fatty acids

Q44. Examples of monounsaturated fatty acids are

a. Oleic acid b. Arachidonic acid
c. Linolenic acid d. Lysine
e. None

Q45. True about prostaglandins is

a. Short acting
b. Present in many tissues
c. Some require CAMP for their action
d. All the true

Q46. Which of the following fatty acid has maxi number of carbon atoms?

a. Oleic acid b. Linolenic acid
c. Arachidonic acid d. Cervonic acid

30. c	31. c	32. c	33. d	34. c	35. d	36. b	37. b	38. b	39. a, b,
40. b	41. a, d	42. c	43. d	44. a	45. d	46. d			

Q47. Which of the following phospholipid has antigenic activity?

a. Plasmalogen
b. Cardiolipin
c. Phosphatidylcholine
d. Sphingomyelin

Q48. Primary bile acid is

a. Deoxycholic acid
b. Lithocholic acid
c. Chenodeoxycnolic acid
d. None

Q49. The major lipid in adipose tissue is:

a. Cholesterol
b. Phospholipids
c. Triglyceride
d. Glyceride

Q50. Which of the following undergoes auto-oxidation?

a. FFA
b. PUFA
c. Chylomicrons
d. Cholestrol

Q51. Immediate precursor of mevalonic acid is

a. Mevalonyl CoA
b. Mevalonyl pyrophosphate
c. Acetoacetyl CoA
d. 3-hydroxy-3-methyglutaryl CoA

Q52. Which of following is not a constituent of ganglioside molecule?

a. Glycerol
b. Sialic acid
c. Lecithins
d. Long chain fatty acid

Q53. Transport of fatty acids from adipose tissues to other tissues for metabolism is primarily a function of:

a. Carnitine
b. Chylomicrons
c. Plasma albumin
d. High density lipoproteins

Q54. Regarding synthesis of triacyl glycerol in adipose tissue, all of the following are true except

a. Synthesis from Dihydroxyacetone phosphate
b. Enzyme Glycerol kinase plays an important role
c. Enzyme Glycerol 3 phosphate dehydrogenase plays an important role
d. Phosphatidate is hydrolyzed

Q55. Basic structure unit from which fatty acids are derived

a. Acetyl CoA
b. Succinyl Coa
c. Acetoacetate
d. Mevalonate

Q56. The following fatty acid does not belong to W6 series

a. Linoleic acid
b. Arachidinic acid
c. Gamma linolenic acid
d. Alpha linolenic acid

Q57. Lipotropic factors are

a. Choline
b. Methionine
c. Chylomicron
d. Pre-alpha-lipoprotein

Q58. Lipogenesis is stimulated by

a. Insulin
b. Glucagon
c. Epinephrine
d. Corticosteroids

Q59. Which of the following is a secondary bile acid?

a. Cholic acid
b. Chenodeoxycholic acid
c. Lithocholic acid
d. None

Q60. Carnitine helps in:

a. Transport of fatty acids to mitochandria to cytosol
b. Transport of fatty acids from cytosol to mitochondria
c. Transport of pyrurate into mitochondria
d. Transport of Malate in Malate shuttle

Q61. Citrate used in fatty acid synthesis used which enzyme

a. Citrate Synthase
b. ATP citrate lyase
c. Aconitase.
d. Malic enzym

Q62. Rate limiting enzyme in Bile acid synthesis is

a. HMG CoA reductase
b. Squalene synthase
c. 7-alpha hydroxylase
d. Isomerase

47. b	48. c	49. c	50. b	51. b	52. a	53. c	54. b	55. a	56. d
57. a, b	58. a	59. c	60. b	61. b	52. c				

Q63. Fatty Acid Synthase complex does not include-

a. Enoyl reductase
b. Keto Acyl Synthase
c. Acetyl Co A carboxylase
d. Acyl tarnsacetylase

Q64. Ketone bodies are synthesized

a. Cytosol b. ER
c. Miochondria d. Peroxisomes

Q65. Minimum fatty acid content is in

a. Safflower oil b. Sunflower oil
c. Peanut oil d. Coconut oil

Q66. Which of the following aids in preventing fatty liver

a. Thiamine
b. Guanidocetate
c. Dietary choline
d. Dimethyl propiothenate

Q67. Ketosis is partly due to:

a. Overutilization of glucose
b. Overproduction of acetyl CoA
c. Under production of acetyl CoA
d. A slowdown in fat metabolism

Q68. Phosoholpids include all except:

a. Plasmalogens b. Dipalmityl lecithin
c. Ceramide d. Cardiolopin

Q69. Which of the following organs cannot use ketone bodies

a. Brain b. Liver
c. Kidney d. Spleen

Q70. True about lipid bilayer of cell wall-

a. Asymmetrical arrangement of cell wall component
b. Lateral diffusion of ions
c. Symmetrical arrangement of cell wall component
d. Not made up of amphipathic lipid

Q71. Beta- oxidation in peroxisome is differentiated form that occurring in mitochondria by:

a. Acetyl CoA
b. H_2O_2 formed
c. Different enzymes are found in different sites NADH is required
d. NADH is required

Q72. Respiratory distress syndrome in premature infants is due to inadequate secretion of which one of the following lipids:

a. Dipalmitoyl phosphatidylcholine
b. Spingomelin
c. Cholesterol
d. Phosphatidylinositol

Q73. Refsum's disease is due to deficiency of which of the following enzyme:

a. Malonate dehydrogenase
b. Thiphorase
c. Succinate thokinase
d. Phytanic alpha oxidase

Q74. Rothera's test used for detection of :

a. Proteins b. Glucose
c. Fatty acid d. Ketones

Q75. ATP yield in palmitic acid oxidation:

a. 106 ATP b. 142 ATP
c. 129 ATP d. 139 ATP

Q76. Ideal total cholesterol to HDL cholesterol ratio is

a. < 1.5 b. <2.5
c. <3.5 d. <4.5

Q77. Triglyerides in serum are transported:

a. HDL b. VLDL
c. LDL d. Chylomicron

Q78. All of the following statements about apoprotien are true except:

a. Apoprotein A – I activates LCAT
b. Apoprotein C-I activates lipoprotein lipase
c. Apoprotein C-II lipoprotein lipase inhibitors
d. Apoprotein C –II activates lipoprotein lipase

Q79. Ligand for LDL

a. APO B 100 b. APO E
c. APO 48 d. APO A 11

Q80. A person on a fat free carbohydrates rich diet continues to grow obese. Which of the following lipoproteins is likely to be elevate in his blood :

a. Chylolomicros b. VLDL
c. LDL d. HDL

63. c	64. c	65. d	66. c	67. b	68. c	69. b	70. a	71. b	72. a
73. d	74. d	75. a	76. c	77. b, d	78. c	79. a	80. b		

Q81. Which of the following has maximum density?

a. VLDL b. LDL
c. HDL d. Chylomicrons

Q82. One of the following is a scavenger of cholesterol from tissue and prevents atherosclerosis:

a. VLDL b. LDL
c. Chylomicrons d. HDL

Q83. The APO-B-48 & APO-B-100 are, main proteins of different lipoproteins due to

a. RNA splicing
b. RNA editing
c. Misreading of mRNA
d. DNA Duplication

Q84. Increased blood levels of cholesterol that are seen in hypothyroidism are most likely due to

a. Decreased calorigenesis
b. Decreased production of LDL receptor in liver and the thus decreased clearance by liver
c. Decreased production of LDL receptor in the adipose tissue and increased release of cholesterol from adipose tissues
d. Increased breakdown of lipoproteins releasing cholesterol in circulation

Q85. Highest quantity of lipid and lowest concentration of protein are found in

a. Chylomicrons
b. Very low density lipoproteins
c. Low density lipoproteins
d. High density lipoproteins

Q86. All of the following statements about lipoprotein lipase are true , except:

a. Found in adipose tissue
b. Found in myocytes
c. Deficiency leads to hyper triacylglyseridemia
d. Does not require CII as cofactor

Q87. Which of the following will be elevated on the bloodstream about 4 hours after eating a high-fat meal?

a. Chylomicrons
b. High-density lipoprotein
c. Ketone bodies
d. Nonesterified fatty acids

Q88. Which of the following is used to transport cholesterol from intestine to liver?

a. Apo E b. Apo C
c. Apo A d. Apo B

Q89. Which form of cholesterol ester is found in plasma most

a. LDL b. HDL
c. VLDL d. Apoprotein-E

Q90. Which receptors are present in liver for uptake of LDL?

a. Apo E
b. Apo A and Apo E
c. Apo E and Apo B 100
d. Apo B 100

Q91. Carrier of cholesterol in plasma is

a. LDL b. VLDL
c. HDL d. Chylomicron

Q92. Which of the following types of hypertriglyceridemia is associated with an increase in chylomicron and VLDL remnants?

a. Type I b. ypes II
c. Type III d. Type IV

Q93. Which of the following is not affected in Abetalipoproteinemia?

a. LD b. VLDL
c. HDL d. IDL

Q94. Type 2 hypercholesterolemia occurs due to

a. Lipoprotein lipase deficiency
b. Absence of LDL receptors on cells
c. Abnormality in apo E
d. LCAT deficiency

Q95. Gangliosides consist of:

a. Long chain fatty acid (LCFA)
b. Alcohol- sphingosine
c. Phosphate
d. Sailic acid
e. Glycerol

81. c	82. d	83. b	84. c	85. a	86. d	87. a	88. d	89. b	90. c
91. a	92. c	93. c	94. b	95. a, b, d					

Q96. To be defined as a ganglioside , a lipid substance isolated from nervous tissue must contain in its structure :

a. N-Acetyineuraminic acid (NANA), hexoses sphingosine , long chain fatty acid
b. NANA, a hexose a fatty acid, sphigosine phosphorylcholine
c. NANA , Phingosine, ethanolamine
d. NANA , hexoses, fatty acid, glycerol

Q97. Enzyme deficient in Tay-sachsdisease

a. Alpha galactosidase
b. Hexosaminidase A
c. Beta galactosidase
d. Gamma glucosidase

Q98. Which organelle is involved in the case of sphinghomyelin deficiency?

a. Mitochondria b. Nucleus
c. Lysosome d. Membrane

Q99. Accumulation of increased amount of sphingomyline in liver and spleen is found in

a. Goucher's disease
b. Niemann-Pick disease
c. Obstructive jaundice
d. VonGierke's disease

Q100. Niemann Pick's disease is due to deficiency of

a. Tyrosinase
b. Glucose-cerebrosidase
c. Sphingomyelinase
d. Hexasaminidase

Q101. Cerebrosides contain which of the following:

a. Phytol b. Glycerol
c. Galactitol d. Sphinogosine

Q102. A membrane phospholipid that does not contain glycerol is

a. Lecithin b. Sphingomyelin
c. Cardiolipin d. Cerarmide

Q103. Gaucher's disease is due to deficiency of enzyme

a. Sphingomyelinase
b. Beta-Glucosidase
c. Hexosaminidase-A
d. Beta-Galactosidase

Q104. Hunter syndrome is due to deficiency of

a. Beta galactosidase
b. Sphingomyelinase
c. Iduronate Sulfatase
d. Hyaluronidase

Q105. Metachromatic leukodystrophy is due to deficiency of

a. Hexosaminidase A
b. Hexosaminidase B
c. Ceramidase
d. Arylsulfatase

96. a	97. b	98. c	99. b	100. c	101. d	102. b	103. b
104. c	105. d						

Lipids – Explanations

1. b) Cell signaling
c) Precursor of Second Messengers
d) Mediators of inflammation
e) Regulate membrane permeability

a. Cell to cell recognition –

Glycoprotein (fibronectin, Iaminin) is involve in cell-cell recognition and adhesion[Ref: Harper's Illustrated biochemistry, 30th Edition]

b. Cell signaling –is done by phospholipids

c. Precursor of Second Messengers –

Phospholipids are the Main Constituents of Membranes

- "Sphingomyelins are found in the outer leaflet of the cell membrane lipid bilayer and are particularly abundant in specialized areas of the plasma membrane known as lipidrafts. They are also found in large quantities in the myelin sheath that surrounds nerve fibers. They are believed to play a role in cell signaling and in apoptosis"- Harper 30th/216
- "Phosphatidylinositol is a Precursor of Second Messengers: The inositol is present in phosphatidylinositol as the stereoisomer, myoinositol. Phosphorylated phosphatidylinositols (phosphoinositides) are minor components of cell membranes, but play an important part in cell signaling and membrane trafficking"-Harper 30th/216

d. Mediators of inflammation –

- The immediate precursor of the eicosinoids is arachidonic acid, present in the beta position of phospholipids in cell membranes and membranes of subcellular particles. Eicosinoids are synthesized via two major pathways:

1. The cyclooxygenase pathway, from which thromboxane A2, prostacyclin (PG12), and PGD2, PGE2 and PGF2 are synthesized and.

2. The 5-lipoxygenase pathway, from which the leukotrienes (LTB4, LTC4, LTD4 and LTE4) are synthesized. Arachidonic acid is hydrolyzed from phospholipids by Phospholipase A2, also a membrane component. Aspirin and other NSAIDs inhibit cyclooxygenase but not lipoxygenase. Anti-inflammatory steroids stabilize membranes and prevent phospholipid hydrolysis thereby inhibiting both pathway- Robbins 9th /83-84.

e. Regulate membrane permeability-

In association with proteins, phospholipids form the structural components of membranes and regulate membrane permeability.

2. a) Phospholipids undergo rapid lateral diffusion
c) Hydrophobic core of the phospholipid bilayer remains constantly in motion because of rotations around the bonds of lipid tails
d) Phospholipids that have one fatty acyl group, cannot form the bilayer

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Phospholipids undergo rapid lateral diffusion-

Membranes are Dynamic Structures

[Ref: Harper's Illustrated biochemistry, 30th Edition]

- Membranes and their components are dynamic structures. Membrane lipids and proteins undergo turnover
- Another indicator of the dynamic nature of membranes is that a variety of studies have shown that lipids and certain proteins exhibit lateral diffusion in the plane of their membranes.
- Many nonmobile proteins do not exhibit lateral diffusion because they are anchored to the underlying actin cytoskeleton. By contrast, the transverse movement of lipids across the membrane (flip-flop) is extremely slow and does not appear to occur at an appreciable rate in the case of membrane proteins.

b. Transverse movement of lipids across the membrane is faster than protein-

"The hydrophobic core of the phospholipid bilayer is constantly in motion because of rotations around the bonds of lipid tails.

Hydrophobic tails of a bilayer bend and lock together. However, because of hydrogen bonding with water, the hydrophilic head groups exhibit less movement as their rotation and mobility are constrained. This results in increasing viscosity of the lipid bilayer closer to the hydrophilic heads"-Wikipedia

c. Hydrophobic core of the phospholipid bilayer remains constantly in motion because of rotations around the bonds of lipid tails

"Some of the intergral membrane proteins span the whole bilayer and they are called transmembrane protein. The transmembrane proteins can serve as receptor, tissue specific antigens, ion channels, membrane-based enzymes, etc."-Vasudevan 5th/12

d. Phospholipids that have one fatty acyl group, cannot form the bilayer- phospholipid has to have 2 fatty acyl groups.

e. Phospholipids span whole bilayer-

Membranes are mainly made up of lipids, proteins and small amount of carbohydrate. Phospholipids are the most common lipids present and they are amphipathic in nature

3. a) Plasminogen

[Ref: Harper's Illustrated Biochemistry, 27th edition]

Explanation:

"**Lipoprotein A, Lp (a)** consists of 1 mol of LDL attached 1 mol of apo(a). Apo(a) shows structural homologies to **plasminogen**."

4. c) Acetyl CoA carboxylase

[Ref: Lippincott Biochemistry, 6th edition]

a. Carnitine palmitoyl transferase 1-is the regulatory step for fatty acid oxidation, which occurs during fasting Fatty acid oxidation occurs in the mitochondrial matrix. Fatty acids have to enter mitochondria for its oxidation.CPT-1 decides the entry of fatty acids into the mitochondria.

b. Pyruvate carboxylase- Pyruvate carboxylase is the first step during gluconeogenesis. Gluconeogenesis is favored by glucagon, the predominanat hormone of the fasting state.

c. Acetyl CoA carboxylase- is the rate-limiting step of fatty acid synthesis. Fatty acid synthesis occurs during well fed state. Insulin is the predominant hormone during well-fed state.

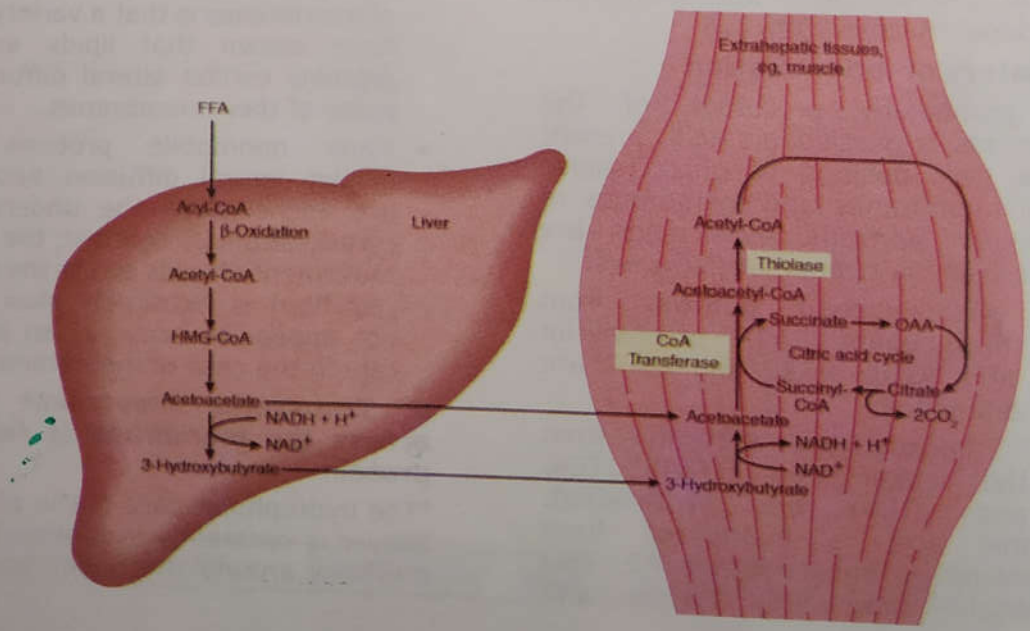
d. HMG lyase-is an enzyme of ketone body synthesis, which occurs during fasting state.

5. a) Thiophorase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Thiophorase-

- SuccinyI-CoA-Acetoacetate-CoA trans-ferase is the actual name of thiophorase.
- As the name suggests , Thiophorase transfers CoA group from succinyl-CoA to acetoacetate, forming acetoacetyl-CoA and Succinate.
- This acetoacetyI-CoA is further acted upon by thiolase to produce 2 molecules of acetyl CoA, which can enter the TCA cycle to produce energy.



Ketone bodies can't be utilised by:

- Thiophorase enzyme is absent in liver, so liver can't utilize ketone bodies.
- Utilization of ketone bodies require mitochondria, so RBCs also can't utilize ketone bodies.

Extra Edge:
HMG coA synthase, not HMG coA lyase is the rate limiting enzyme of ketogenesis.
HMG coA synthase of cholesterol synthesis is located in cytoplasm.
HMG coA synthase of ketogenesis is located in mitochondria.

b. HMGCoA lyase-

It is involved in ketone body synthesis

c. HMG-CoA reductase-

It is the rate limiting enzyme of cholesterol biosynthesis

d. Succinate dehydrogenase-

- It is a FAD dependant enzyme of TCA cycle and electron transport chain.
- It is the only enzyme of TCA cycle located in the mitochondrial membrane while other enzymes are located in matrix.
- It is inhibited by malonate.

6. b) HMG CoA synthase

[Ref: Lippincott's illustrated reviews, 6th Edition]

Explanation:

- HMG CoA synthases enzyme is common to both pathways.

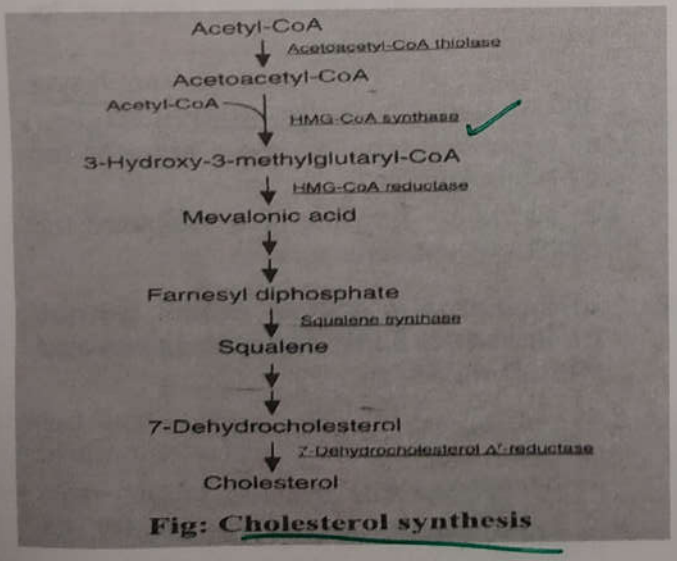


Fig: Cholesterol synthesis

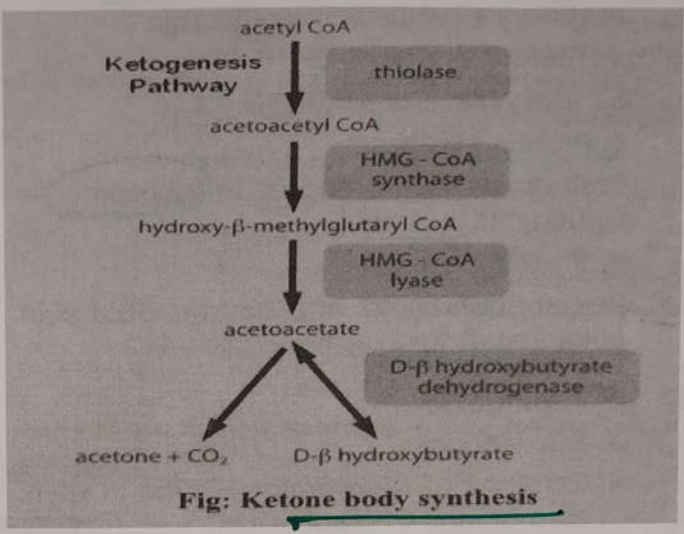


Fig: Ketone body synthesis

Note:

- Mitochondrial HMG CoA used for ketogenesis.
- Cytosolic HMG CoA used for cholesterol synthesis

7. a) Mitochondria

[Ref: Lippincott's illustrated reviews, 6th Edition]

Mechanism of catabolism	Chief organelle	Fatty acids
Beta oxidation	Mitrochondria	Long chain fatty acids Medium chain fatty acids Short chain fatty acids
Beta oxidation	Peroxisomes	Very long chain fatty acids
Omega oxidation	Endoplasmic reticulum	Works only when mitochondria does not oxidize
Alpha oxidation	Peroxisomes	Branched chain fatty acids

8. b) Triacylglycerol synthesis

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Glycolysis-

Glycolysis occurs in cytosol → option a is excluded.

b. Triacylglycerol synthesis –

Functions of endoplasmic reticulum

1. Final step of gluconeogenesis
2. Phase I biotransformation reactions.

3. N-glycosylation begins (O-glycosylation exclusively happens in golgi).

4. Steroid synthesis

5. Triacylglycerol synthesis

c. Protein synthesis –

Protein synthesis occurs in ribosome → Option c is excluded

d. Protein packaging -

Protein packaging and sorting occurs in golgi apparatus.

9. a) β-oxidation

a. β-oxidation-

- Carnitine (β-hydroxy-γ-trime thyl-ammonium butyrate), $(CH3)3\ N^{+}\ 'CH2\ 'CH(OH)\ 'CH2\ 'COO-$, is widely distributed and is particularly abundant in muscle. Long-chain acyl-CoA (or FFA) cannot penetrate the inner membrane of mitochondria.
- In the presence of carnitine, however, carnitine palmitoyltransferase-I, located in the outer mitochondrial membrane, transfers long-chain acyl group from CoA to carnitine, forming acylcarnitine and releasing CoA.
- Acylcarnitine is able to penetrate the inner membrane and gain access to the β-oxidation system of enzymes via the inner membrane exchange transporter carnitine-acylcarnitine translocase.
- The transporter binds acylcarnitine and transports it across the membrane in exchange for carnitine. The acyl group is then transferred to CoA so that acyl-CoA is reformed and carnitine is liberated. This reaction is catalyzed by carnitine palmitoyltransferase-II, which is located on the inside of the inner membrane.

b. Ketonebody formation from acetylCoA-occurs in ketogenesis, does not require carnitine.

c. Palmitate synthesis-This is fatty acid synthesis, does not require carnitine.

d. Mobilization of stored triacylglycerols from adipose tissue - does not require carnitine.

10. c) Arginine

One type of fatty liver that has been studied extensively in rats is caused by a deficiency of choline, which has therefore been called a lipotropic factor. The antibiotic puromycin, ethionine (α-amino-γ-mercaptobutyric acid), carbon tetrachloride, chloroform, phosphorus, lead, and arsenic all cause fatty liver and a marked reduction in concentration of VLDL in rat blood. Choline will not protect the organism against these agents, but appears to aid in recovery. The action of carbon tetrachloride probably involves formation of free radicals causing lipid peroxidation. Some protection against this is provided by the antioxidant action of vitamin E-supplemented diets. The action of ethionine is thought to be caused by a reduction in availability of ATP due to its replacing methionine in S-adenosylmethionine, trapping available adenine and preventing synthesis of ATP. Orotic acid also causes fatty liver; it is believed to interfere with glycosylation of the lipoprotein, thus inhibiting release, and may also impair the recruitment of triacylglycerol to the particles. A deficiency of vitamin E enhances the hepatic necrosis of the choline deficiency type of fatty liver. Added vitamin E or a source of selenium has a protective effect by combating lipid peroxidation. In addition to protein deficiency, essential fatty acid and vitamin deficiencies (eg, linoleic acid, pyridoxine, and pantothenic acid) can cause fatty infiltration of the liver.

a. Choline -is a lipotropic factor

b. Lecithine - is a lipotropic factor

c. Arginine- is not a lipotropic factor

d. Methionine - is a lipotropic factor

11. b) Lysine

a. Alanine –alanine is not required for carnitine synthesis.

b. Lysine –carnitine is formed from lysine and methionine. In liver and kidney.

c. Arginine - Arginine is not required for carnitine synthesis.

d. Tyrosine - Tyrosine is not required for carnitine synthesis.

12. c) In humans double bonds cannot be introduced into fatty acids beyond the Δ9 position.

a. It is an ω3 fatty acid.-this is true but is not responsible for its essential nature.

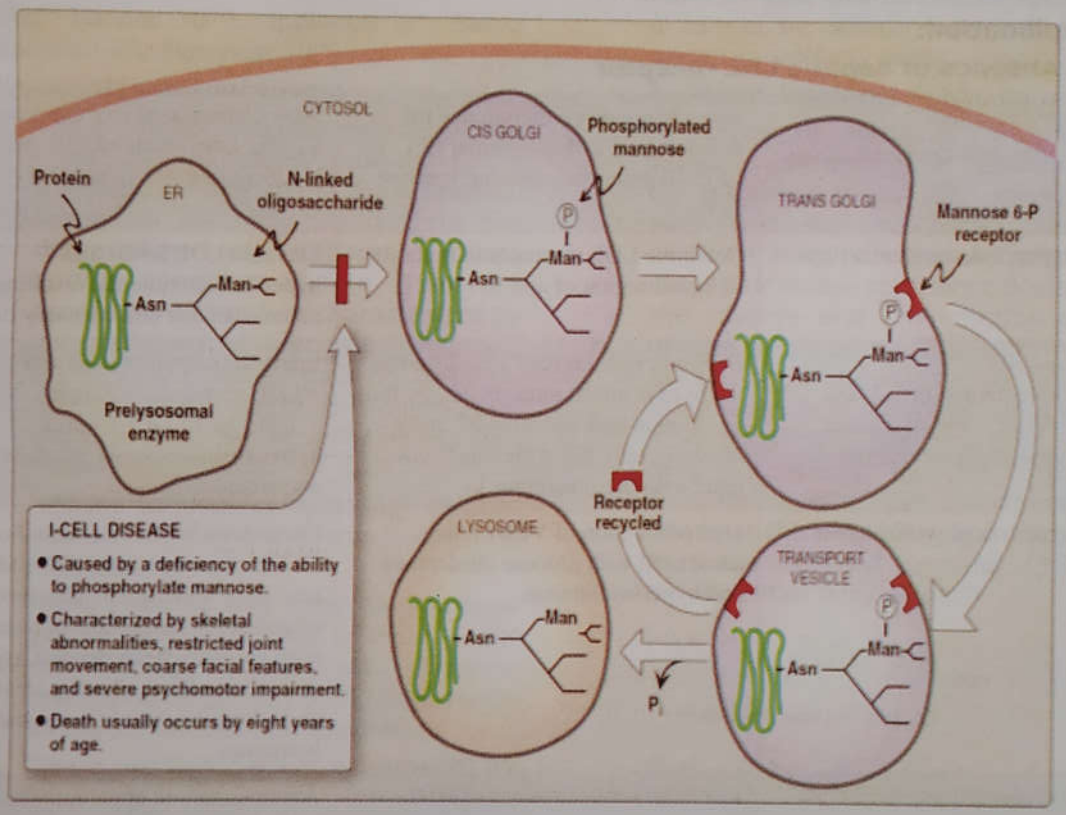
b. It contains three double bonds.- this is true but is not responsible for its essential nature.

c. In humans double bonds cannot be introduced into fatty acids beyond the Δ9 position.

Linoleic and α-linolenic acids are the only fatty acids known to be essential for the complete nutrition of many species of animals, including humans, and are termed the nutritionally essential fatty acids. In most mammals, arachidonic acid can be formed from linoleic acid. Double bonds can be introduced at the Δ4, Δ5, Δ6, and Δ9 positions in most animals, but never beyond the Δ9 position. In contrast, plants are able to synthesize the nutritionally essential fatty acids by introducing double bonds at the Δ12 and Δ15 positions.

d. In humans double bonds cannot be introduced into fatty acids beyond the Δ12 position.-this is false

13. b) Lysosomes



a. Golgi apparatus-is not involved

b. Lysosomes- Mutations in the gene encoding GlcNAc phosphotransferase, resulting in absence of the Man 6-P signal for lysosomal localization of certain hydrolases.

c. Peroxisomes - are not involved

d. Mitochondria - is not involved

14. b) 120ATP

a. 146 ATP

b. 120ATP - The breakdown of stearic acid (C18) requires 8 cycles of β-oxidation each producing 1 FADH2 and 1 NADH molecule and results in the formation of Nine 2C acetyl CoA molecules.

c. 129 ATP

d. 139 ATP

15. b) Muscle

a. RBC-can use only glucose. Red blood cells lack mitochondria, and hence the enzymes of the TCA cycle, electron transport chain, β-oxidation pathway, or ATP synthase. This renders them incapable of utilizing fatty acids or ketone bodies as metabolic fuel. Consequently, red blood cells are completely reliant of glycolysis to generate ATP.

b. Muscle- **can metabolize glucose, fatty acids, and ketone bodies for ATP production.**

In extrahepatic tissues, acetoacetate is activated to acetoacetyl-CoA by succinyl-CoA-acetoacetate CoA transferase. CoA is transferred from succinyl-CoA to form acetoacetylCoA . With the addition of a CoA, the acetoacetyl-CoA is split into two acetyl-CoAs by thiolase and oxidized in the citric acid cycle. If the blood level is raised, oxidation of ketone bodies increases until, at a concentration of ~12 mmol/L, the oxidative machinery is saturated. When this occurs, a large proportion of oxygen consumption may be accounted for by the oxidation of ketone bodies.

c. Hepatocytes - cant use ketone bodies because of lack of enzyme thiophorase.

d. Brain-can use ketone bodies after 2-3 days of starvation.

16. b) Absence of hepatic LDL receptor

Explanation:

b. Absence of hepatic LDL receptor

Hyperlipoproteinemias Familial lipoprotein lipase deficiency (type 1)	Hypertriacylglycerolemia due to deficiency of LPL, abnormal LPL, or apo C-ll deficiency causing Inactive LPL.	Slow clearance of chylomicrons and VLDL. Low levels of LDL and HDL. No increased risk of coronary disease.
Familial hypercholesterolemia (type lla)	Defective LDL receptors or mutation in ligand region of apo B-100.	Elevated LDL levels and hypercholesterolemia, resulting in atherosclerosis and coronary disease.
Familial type III hyperlipoproteinemia (broad beta disease, remnant removal disease, familial dysbetalipoproteinemia	Deficiency in remnant clearance by the liver is due to abnormality in apo E. Patients lack isoforms E3 and E4 and have only E2, which does not react with the E receptor.1	Increase in chylomicron and VLDL remnants of density < 1.019 (p VLDL). Causes hypercholesterolemia, xanthomas, and atherosclerosis.
Familial hypertriacylglycerolemia (type IV)	Overproduction of VLDL often associated with glucose intolerance and hyperinsulinemia.	Cholesterol levels rise with the VLDL concentration. LDL and HDL tend to be subnormal. This type of pattern is commonly associated with coronary heart disease, type II diabetes mellitus, obesity, alcoholism, and administration of progestational hormones.
Familial hyperalphalipoproteinemia	Increased concentrations of HDL.	A rare condition apparently beneficial to health and longevity.

Disorder	Defect
Familial lipoprotein lipase deficiency (type 1)	LDL, or apo C-II
Familial hypercholesterolemia (type IIa)	LDL receptor or apoB-100
Familial type III hyperlipoproteinemia	Apo E
Familial hypertriacylglycerolemia (type IV)	VLDL over production

EXTA EDGE:

Mechanism of action of hypolipidemic drugs:

Statins	Competitive inhibitor of HMG CoA reductase
Ezetimibe	Inhibits intestinal cholesterol absorption (inhibits Niemann-Pick C1-like 1-NPC1L1)
Cholestyramine (Bile acid binding resin)	Excretion of bile acids in the stool

Fibrates	PPARα activator (↓TG synthesis in liver)
Niacin	↓ lipolysis in adipocytes; ↓ VLDL; ↑ HDL

17. a) It is a type of lysosomal storage disorder
c) Skeletal defect is manifested as dystosis multiplex
d) Research is going on to develop give therapy for Morquio syndrome

[Ref: Harper 30th& Lippincott 6th; Satya Narayan 4th; Harrison 19th]

Mucopolysaccharidoses:

- The mucopolysaccharidoses are hereditary diseases caused by a deficiency of any one of the lysosomal hydrolase normally involved in the degradation of heparan sulfate and/or dermatan sulfate. They are progressive disorders characterized by accumulation of glycosaminoglycans in various tissues, causing a range of symptoms, such as skeletal and extracellular matrix deformities, and mental retardation.
- All are autosomal recessive disease except Hunter syndrome, which is X-linked.
- Bone marrow and cord blood transplants have been used to treat Hurler and Hunter syndromes. Enzyme replacement therapy (ERT) is currently available for both syndromes.
- There are two current treatments for the MPS I diseases. Hematopoietic stem cell transplantation (HSCT) is the standard treatment for patients presenting at <2 years of age who appear to have or are at risk for neurologic degeneration.
- A combination of enzyme therapy and HSCT has been used, with enzyme therapy initiated prior to transplantation in an attempt to reduce the disease burden.
- The experience with this approach is not well documented, but it appears to have advantages over HSCT alone. Enzyme therapy for Maroteaux-Lamy disease (MP8 VI) has received US. FDA approval.
- HSCT has not been successful in treating CNS disease associated with MP5 II. The FDA and the European Medicines Agency (EMA) have approved enzyme therapy for the visceral manifestations of MPS II.

18. a) Palmitic acid
b) Alpha-linolenic acid

[Ref: Harper 30th& Lippincott 6th Edition]

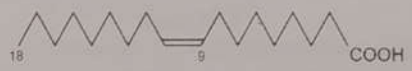
a. Palmitic acid-

Palmitic acid is a saturated fatty acid.so it cannot be omega fatty acid ,which is unsaturated fatty acids.

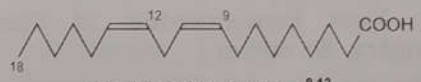
b. Alpha-linolenic acid-

Structure of some unsaturated fatty acids. Although the carbon atoms in the molecules are conventionally numbered—ie, numbered from the carboxyl terminal—the ω numbers (eg, ω7 in palmitoleic acid) are calculated from the reverse end (the methyl terminal) of the molecules. The information in parentheses shows, for instance, that α-linolenic acid contains double bonds starting at the third carbon from the methyl terminal, has 18 carbons and 3 double bonds, and has these double bonds at the 9th, 12th, and 15th carbons from the carboxyl terminal. (*Classified as "essential fatty acids.")

Palmitoleic acid (ω7, 16:1, Δ^9)

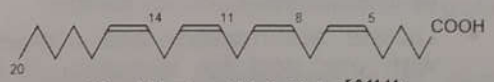


Oleic acid (ω9, 18:1, Δ^9)

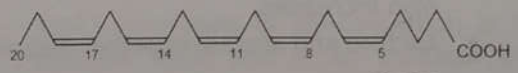


*Linoleic acid (ω6, 18:2, $\Delta^{9,12}$)

*α-Linolenic acid (ω3, 18:3, $\Delta^{9,12,15}$)



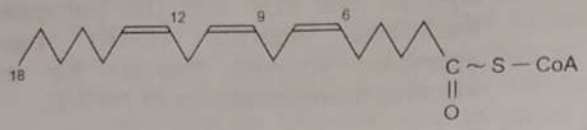
*Arachidonic acid (ω6, 20:4, $\Delta^{5,8,11,14}$)



Eicosapentaenoic acid (ω3, 20:5, $\Delta^{5,8,11,14,17}$)

c. Linoleic acid-see option b

d. Gamma linolenic acid-see option b



γ-Linolenoyl-CoA ($\Delta^{6,9,12}$-octadecatrienoyl-CoA)

e. Arachidonic acid-see option b

19. a) Apo A I
b) Apo A II

e) Apo D

[Ref: Harper 30th; Lippincott 6th; Satyanarayan 4th]

a. Apo A I-is associated with HDL

b. Apo A II-is associated with HDL

c. Apo B-48-is associated with CHYLOMICRON

d. Apo 100-is associated with LDL,VLDL

e. Apo D-is associated with HDL

Major apolipoproteins

Apolipoproteins	Functional activity	Lipoprotein carrier (s)
Apo A-I	Cofactor LCAT	Chylomicron, HDL
Apo A-II	Not known	HDL
Po A-IV	Activation of LCAT Secretion of triglyceride from liver binding protein to LDL receptor	Chylomicron, HDL
Apo B-48	Secretion of triglyceride from intestine	Chylomicron
Apo B-100	Cholesterol transport from liver	LDL
Apo C-I	Activation of LCAT (?)	Chylomiron, VLDL, HDL
Apo C-II	Cofactor of LPL	Chylomiron, VLDL, HDL
Apo C-III	Inhibition of apo CIII, activation of LPL	Chylomiron, VLDL, HDL
Apo D	Unknown	HDL
Apo E	Facilitation of uptake of chylomicron remnant and LDL	Chylomiron, VLDL, HDL
Apo (a)	Unknown	Lp (a)

20. d) Alcoholism

[Ref: Tietz Fundamentals of Clinical Chemistry, 6th edition]

- The increase may be even higher in diabetics. More commonly, inhibition of gluconeogenesis occurs and becomes apparent as hypoglycaemia and ketonemia as ethanol is metabolised to acetaldehyde and to acetate.
- Lactate accumulates and competes with uric acid for excretion in the kidneys so that the serum uric acid is also increased.
- Lactate and acetate together decrease the plasma bicarbonate, leading to metabolic acidosis. When moderate amounts of alcohol are ingested for 1 week, the serum triglyceride concentration is increased by more than 20 mg/dL (0.23 mmol/L).
- Prolonged moderate ingestion of alcohol my increase the HDL cholesterol concentration, which is associated with reduced plasma concentration of cholesterol ester transfer protein (CETP).
- Phenols in wine with potent antioxidant activity are probably responsible for reducing the oxidation of LDL cholesterol.

21. a) Chylomicron

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Apolipoprotein

- The major apolipoproteins of HDL (α-lipoprotein) are apoAs.
- The main apolipoprotein of:
- LDL (β-lipoprotein) and VLDL is apo B (B-100).
- Chylomicrons contain a truncated form of apo B (B-48).
- Apo B (B-48) synthesized in the intestine, while B-100 is synthesized in the liver.
- Apo B-48 (48% of B-100) is formed after transcription of the apo B-100 gene by the introduction of a stop signal into the mRNA transcript by an RNA editing enzyme.
- Apos C-I, C-II and C-III are smaller polypeptides (molecular mass 7000-9000 Da) freely transferable between several different lipoproteins.
- Apo E, found in VLDL, HDL, chylomicrons, and chylomicron remnants, is also freely transferable; it accounts for 5% to 10% of total VLDL apolipoproteins in normal subjects.

22. c) Bile salts

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Pancreatic lipase-

Pancreatic lipase is secreted into the small intestine and requires a further pancreatic protein, colipase, for activity. It is specific for the primary ester links—ie, positions 1 and 3 in triacylglycerols—resulting in 2-monoacylglycerols and free fatty acids as the major end products of luminal triacylglycerol digestion. Inhibitors of pancreatic lipase are used to inhibit triacylglycerol hydrolysis in the treatment of severe obesity. Pancreatic esterase in the intestinal lumen hydrolyzes monoacylglycerols, but they are poor substrates, and only ~25% of ingested triacylglycerol is completely hydrolyzed to glycerol and fatty acids before absorption

b. Gastric lipase-

Hydrolysis of triacylglycerols is initiated by lingual and gastric lipases, which attack the sn-3 ester bond forming 1,2-diacylglycerols and free fatty acids, which act as emulsifying agents.

c. Bile salts -

Bile salts, formed in the liver and secreted in the bile, permit emulsification of the products of lipid digestion into micelles together with dietary phospholipids and cholesterol secreted in the bile (about 2 g/d) as well as dietary cholesterol (about 0.5 g/d). Micelles are less than 1 μm in diameter, and soluble, so they allow the products of digestion, including the fat-soluble vitamins, to be transported through the aqueous environment of the intestinal lumen to come into close contact with the brush border of the mucosal cells, allowing uptake into the epithelium. The bile salts remain in the intestinal lumen, where most are absorbed from the ileum into the enterohepatic circulation.

In the alkaline bile (pH 7.6-8.4), the bile acids and their conjugates are assumed to be in a salt form—hence the term "bile salts."

d. Bile pigments-

Heme is synthesized from porphyrins and iron, and the products of degradation of heme are the bile pigments and iron.

23. c) Citrate

a. Malonyl CoA

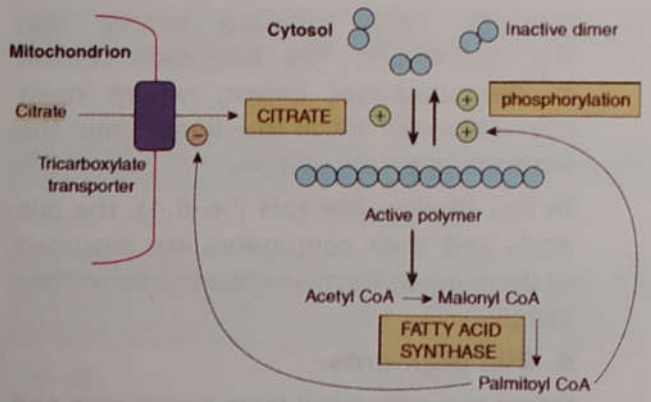
b. Acetyl CoA

c. Citrate

Acetyl-CoA Carboxylase Is the Most Important Enzyme in the Regulation of Lipogenesis

Acetyl-CoA carboxylase is an allosteric enzyme and is activated by citrate, which increases in concentration in the well-fed state and is an indicator of a

plentiful supply of acetylCoA. Citrate promotes the conversion of the enzyme from an inactive dimer (two subunits of the enzyme complex) to an active polymeric form, with a molecular mass of several million. Inactivation is promoted by phosphorylation of the enzyme and by long-chain acyl-CoA molecules, an example of negative feedback inhibition by a product of a reaction (Figure 23–6). Thus, if acyl-CoA accumulates because it is not esterified quickly enough or because of increased lipolysis or influx of free fatty acids into the tissue, it will automatically reduce the synthesis of new fatty acid. Acyl-CoA also inhibits the mitochondrial tricarboxylate transporter, thus preventing activation of the enzyme by egress of citrate from the mitochondria into the cytosol .Acetyl-CoA carboxylase is also regulated by hormones such as glucagon, epinephrine, and insulin via changes in its phosphorylation state.



Regulation of acetyl CoA carboxylase.

AcetylCoA carboxylase is activated by citrate, which promotes the conversion of the enzyme from an inactive dimer to an active polymeric form. Inactivation is promoted by phosphorylation of the enzyme and by long-chain acyl-CoA molecules such as palmitoyl CoA. In addition, acyl-CoA inhibits the tricarboxylate transporter, which transports citrate out of mitochondria into the cytosol, thus decreasing the citrate concentration in the cytosol and favoring inactivation of the enzyme.

d. Biotin

24. b) Propionyl CoA

a. Succinyl CoA

b. Propionyl CoA-

Oxidation of a Fatty Acid With an Odd Number of Carbon Atoms Yields Acetyl-CoA Plus a Molecule of Propionyl-CoA

Fatty acids with an odd number of carbon atoms are oxidized by the pathway of β-oxidation described above producing acetyl CoA until a three-carbon (propionyl-CoA) residue remains. This compound is converted to succinyl-CoA, a constituent of the citric acid cycle .Hence, the propionyl residue from an odd-chain fatty acid is the only part of a fatty acid that is glucogenic.

c. Acetyl CoA

d. Malonyl CoA

25. b) LDL

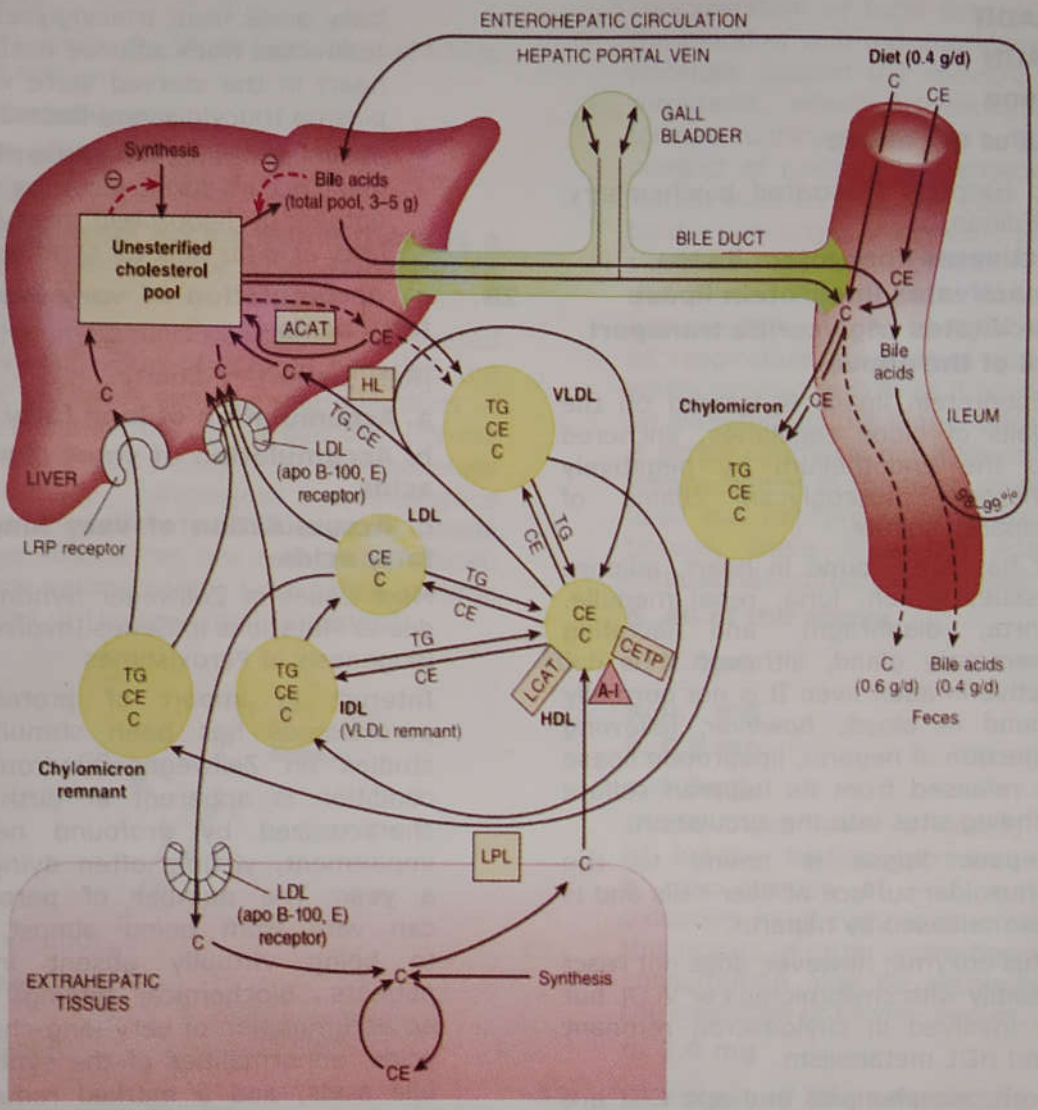
[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. VLDL

b. LDL-

CHOLESTEROL IS TRANSPORTED BETWEEN TISSUES IN PLASMA LIPOPROTEINS

Cholesterol is transported in plasma in lipoproteins, with the greater part in the form of cholesteryl ester ,and in humans the highest proportion is found in LDL. Dietary cholesterol equilibrates with plasma cholesterol in days and with tissue cholesterol in weeks. Cholesteryl ester in the diet is hydrolyzed to cholesterol, which is then absorbed by the intestine together with dietary unesterified cholesterol and other lipids. With cholesterol synthesized in the intestines, it is then incorporated into chylomicrons . Of the cholesterol absorbed, 80% to 90% is esterified with long-chain fatty acids in the intestinal mucosa. Ninety-five percent of the chylomicron cholesterol is delivered to the liver in chylomicron remnants, and most of the cholesterol secreted by the liver in very low density lipoprotein (VLDL) is retained during the formation of intermediate-density lipoprotein (IDL) and ultimately LDL, which is taken up by the LDL receptor in liver and extrahepatic tissues.



c. Chylomicrons

d. HDL

e. All of the above

26. a) NADPH

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. NADPH-

The Main Source of NADPH for Lipogenesis Is the Pentose Phosphate Pathway

NADPH is involved as a donor of reducing equivalents in both the reduction of the 3-ketoacyl and of the 2,3-unsaturated acyl derivatives . The oxidative reactions of the pentose phosphate pathway are the chief source of the hydrogen required for the reductive synthesis of fatty acids. Significantly, tissues specializing in active lipogenesis—ie, liver, adipose tissue, and the lactating mammary gland— also possess an active pentose phosphate pathway. Moreover, both metabolic pathways are found in the cytosol of the cell; so, there are no membranes or permeability barriers against the transfer of NADPH. Other sources of NADPH include the reaction that converts malate to pyruvate catalyzed by the "malic enzyme" (NADP malate dehydrogenase) and the extramitochondrial isocitrate dehydrogenase reaction (probably not a substantial source, except in ruminants).

b. NADH

c. FADH

d. None

27. d) All of the above

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Activates lipoprotein lipase

b. Inactivates lipoprotein lipase

c. Facilitates triglyceride transport

d. All of the above-

- Lipoprotein lipase is located on the walls of blood capillaries, anchored to the endothelium by negatively charged proteoglycan chains of heparan sulfate.
- It has been found in heart, adipose tissue, spleen, lung, renal medulla, aorta, diaphragm, and lactating mammary gland, although it is not active in adult liver. It is not normally found in blood; however, following injection of heparin, lipoprotein lipase is released from its heparan sulfate binding sites into the circulation.
- Hepatic lipase is bound to the sinusoidal surface of liver cells and is also released by heparin.
- This enzyme, however, does not react readily with chylomicrons or VLDL but is involved in chylomicron remnant and HDL metabolism.
- Both phospholipids and apo C-II are required as cofactors for lipoprotein lipase activity, while apo A-II and apo C-III act as inhibitors.
- Hydrolysis takes place while the lipoproteins are attached to the enzyme on the endothelium.
- Triacylglycerol is hydrolyzed progressively through a diacylglycerol to a monoacylglycerol and finally to FFA plus glycerol.
- Some of the released FFA return to the circulation, attached to albumin, but the bulk is transported into the tissue .
- Heart lipoprotein lipase has a low Km for triacylglycerol, about one-tenth of that for the enzyme in adipose tissue. This enables the delivery of fatty acids from triacylglycerol to be redirected from adipose tissue to the heart in the starved state when the plasma triacylglycerol decreases.
- A similar redirection to the mammary gland occurs during lactation, allowing uptake of lipoprotein triacylglycerol fatty acid for milk fat synthesis.

28. c) Accumulation of very long chain fatty acids

[Ref: Stryer 8th Edition]

a. Accumulation of long fatty acids

b. Accumulation of short chain fatty acids

c. Accumulation of very long chain fatty acids-

Most Cases of Zellweger Syndrome Are due to Mutations in Genes Involved in the Biogenesis of Peroxisomes

Interest in import of proteins into peroxisomes has been stimulated by studies on Zellweger syndrome. This condition is apparent at birth and is characterized by profound neurologic impairment, victims often dying within a year. The number of peroxisomes can vary from being almost normal to being virtually absent in some patients. Biochemical findings include an accumulation of very-long-chain fatty acids, abnormalities of the synthesis of bile acids, and a marked reduction of plasmalogens. The condition is usually caused by mutations in genes encoding certain proteins—the PEX family of genes, also called peroxins —involved in various steps of peroxisome biogenesis (such as the import of proteins described above), or in genes encoding certain peroxisomal enzymes themselves. Two closely related conditions are neonatal adrenoleukodystrophy and infantile Refsum disease. Zellweger syndrome and these two conditions represent a spectrum of overlapping features, with Zellweger syndrome being the most severe (many proteins affected) and infantile Refsum disease the least severe (only one or a few proteins affected).

d. Accumulation of medium chain fatty acids

29. c) Fat

[Ref: Harper's Illustrated biochemistry, 30th Edition]

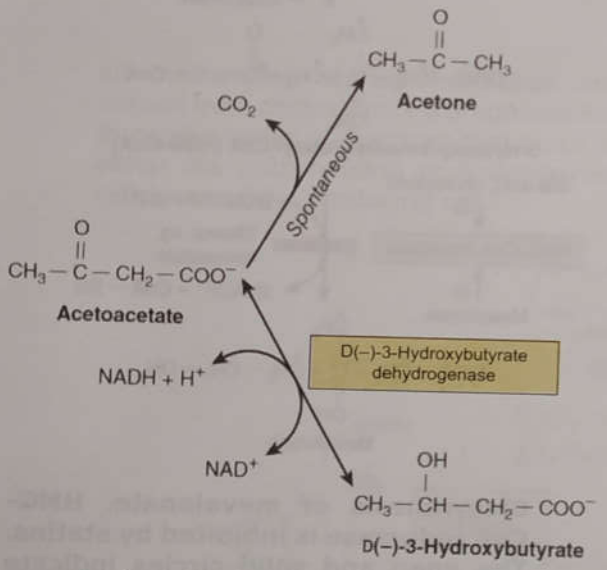
a. Carbohyrate

b. Protein

c. Fat

Ketogenesis occurs when there is a high rate of fatty acid oxidation in the liver

Under metabolic conditions associated with a high rate of fatty acid oxidation, the liver produces considerable quantities of acetoacetate and d(-)-3-hydroxybutyrate (β-hydroxybutyrate). Acetoacetate continually undergoes spontaneous decarboxylation to yield acetone. These three substances are collectively known as the ketone bodies (also called acetone bodies or [incorrectly*] "ketones").



Acetoacetate and 3-hydroxybutyrate are interconverted by the mitochondrial enzyme d(−)-3-hydroxybutyrate dehydrogenase; the equilibrium is controlled by the mitochondrial [NAD+]/[NADH] ratio, that is, the redox state. The concentration of total ketone bodies in the blood of well-fed mammals does not normally exceed 0.2 mmol/L except in ruminants, where 3-hydroxybutyrate is formed continuously from butyric acid (a product of ruminal fermentation) in the rumen wall. In vivo, the liver appears to be the only organ in nonruminants to add significant quantities of ketone bodies to the blood. Extrahepatic tissues utilize acetoacetate and β-hydroxybutyrate as respiratory substrates. Acetone is a waste product which, as it is volatile, can be excreted via the lungs. Because there is active synthesis but little utilization of ketone bodies in the liver, while they are used but not produced in extrahepatic tissues, there is a net flow of the compounds to the extrahepatic tissues.

d. All of the above

30. c) 1.0mg

a. 0.1 mg

b. 0.5 mg

c. 1.0mg-

If the blood level is raised, oxidation of ketone bodies increases until, at a concentration of ~12 mmol/L, the oxidative machinery is saturated. When this occurs, a large proportion of oxygen consumption may be accounted for by the oxidation of ketone bodies.

d. 2.0 mg

31. c) Excess of bile salts in the urine

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Excess of urobilinogen in urine

b. Excess of unconjugated serum bilirbin

c. Excess of bile salts in the urine

Laboratory Results in Normal Patients and Patients With Three Different Causes of Jaundice:

Condition	Serum Bilirubin	Urine Urobilinogen	Urine Bilirubin	Fecal Urobilinogen
Normal	Direct: 0.1-0.4 mg/dL	0-4 mg/24 h	Absent	40-280 mg/24 h
	Indirect: 0.2-0,7 mg/dL			
Hemolytic anemia	↑ Indirect	Increased	Absent	Increased

Hepatitis	↑ Directand indirect	Decreased if micro-obstruction is present	Present if micro-obstruction occurs	Decreased
Obstructive jaundice	↑ Direct	Absent	Present	Trace to absent

The most common causes of obstructive (posthepatic) jaundice are cancer of the head of the pancreas and a gallstone lodged in the common bile duct. The presence of bilirubin in the urine is sometimes referred to as choluria—therefore, hepatitis and obstruction of the common bile duct cause choluric jaundice, whereas the jaundice of hemolytic anemia is referred to as acholuric. The laboratory results in patients with hepatitis are variable, depending on the extent of damage to parenchymal cells and the extent of micro-obstruction to bile ductules. Serum levels of alanine aminotransferase and aspartate aminotransferase are usually markedly elevated in hepatitis, whereas serum levels of alkaline phosphatase are elevated in obstructive liver disease.

d. All of the above

32. c) HMG CoA reductase

a. HMG CoA synthetase

b. HMG CoA oxygenase

c. HMG CoA reductase

The drugs compactin and lovastatin (mevinolin) are fungal products. They are used to decrease the serum cholesterol level in patients with hypercholesterolemia. Compactin and lovastatin are competitive inhibitors of the enzyme HMG CoA reductase and, therefore, reduce cholesterol synthesis. About 50 to 60% decrease in serum cholesterol level has been reported by a combined use of these two drugs.

d. HMG CoA hydratase

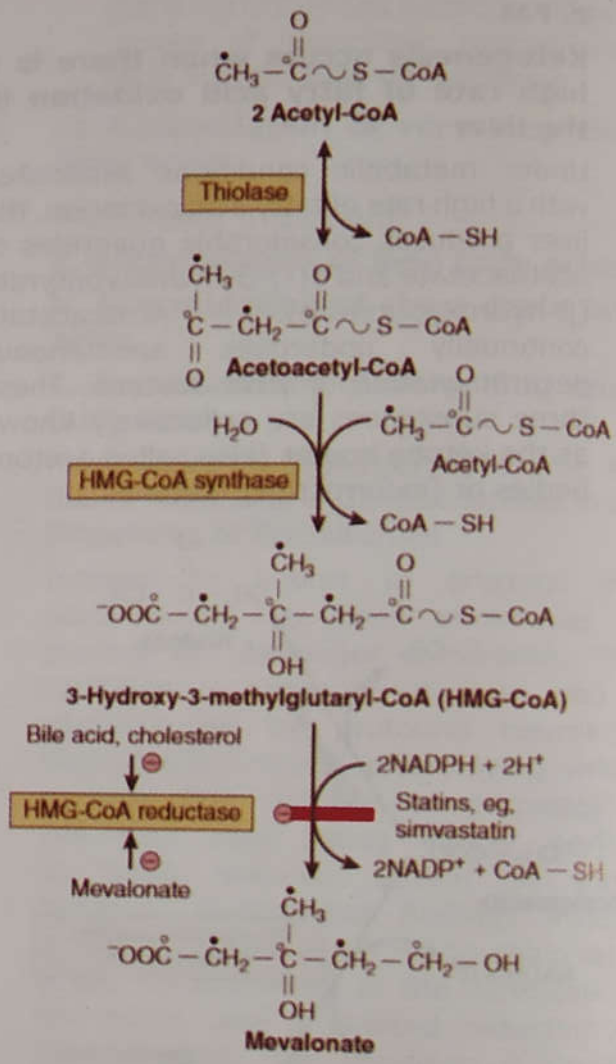
e. HMGCoAmutase

33. d) Pyruvate

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Cholesterol **b. Mevalonate**

c. Acetyl Co A **d. Pyruvate**



Biosynthesis of mevalonate. HMG-CoA reductase is inhibited by statins. The open and solid circles indicate the fate of each of the carbons in the acetyl moiety of acetyl-CoA.

34. c) Coprostanol

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Cholic acid-

The primary bile acids are synthesized in the liver from cholesterol. These are cholic acid (found in the largest amount in most mammals) and chenodeoxycholic acid

b. Glycine –

glycine, the smallest amino acid, can be

accommodated in places inaccessible to other amino acids, it often occurs where peptides bend sharply.

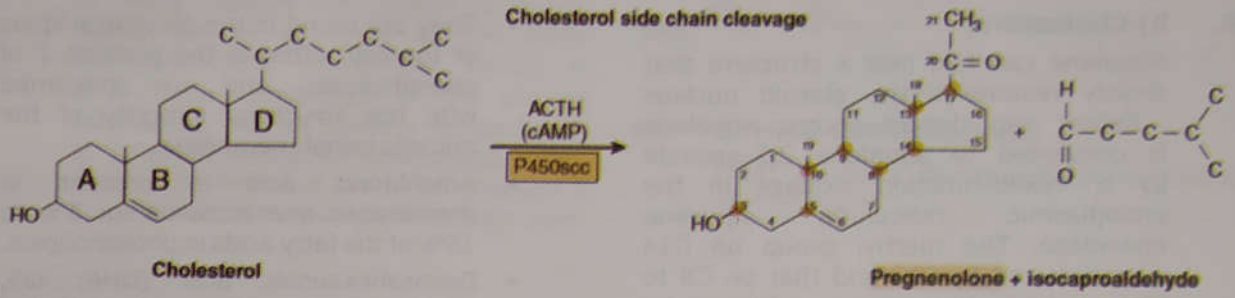
Glycine is formed in the body:

Glycine aminotransferases can catalyze the synthesis of glycine from glyoxylate and glutamate or alanine. Unlike most aminotransferase reactions, these strongly favor glycine synthesis. Additional important mammalian routes for glycine formation are from choline and from serine.

c. Coprostanol-

Cholesterol is excreted from the body via the bile either in the unesterified form or after conversion into bile acids in the liver. Coprostanol is the principal sterol in the feces; it is formed from cholesterol by the bacteria in the lower intestine.

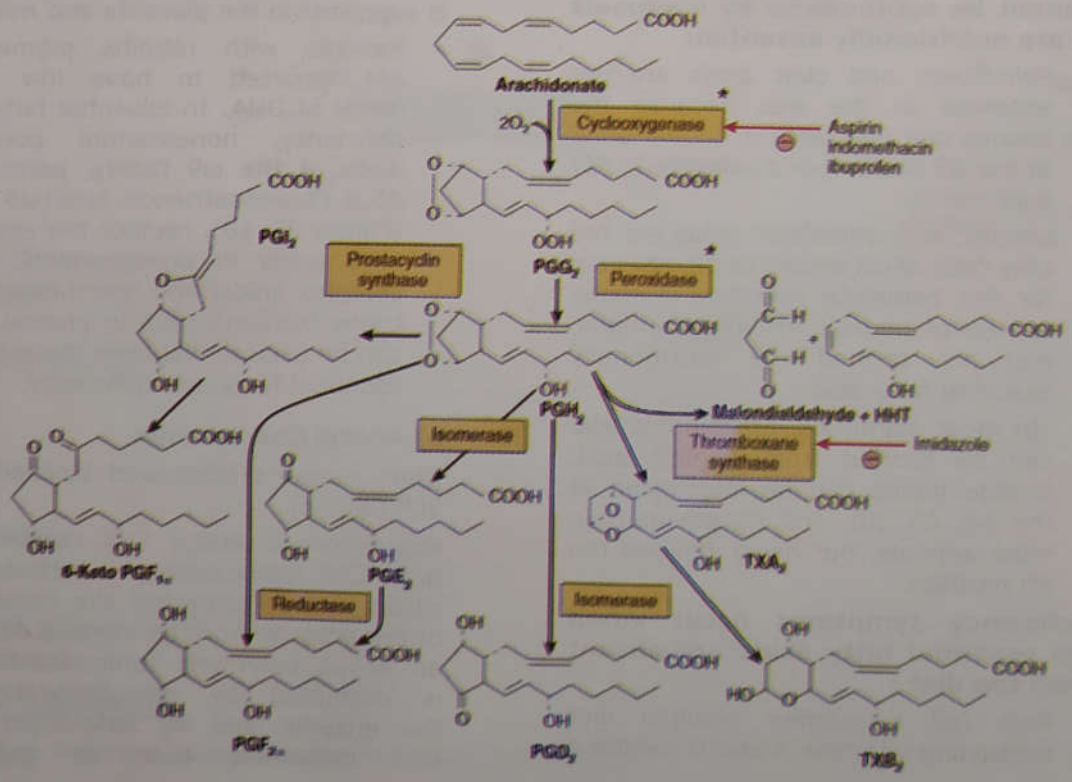
d. Pregnenolone-



All mammalian steroid hormones are formed from cholesterol via pregnenolone through a series of reactions that occur in either the mitochondria or endoplasmic reticulum of the producing cell.

35. d) Leukotriene and prostaglandin

[Ref: Harper's Illustrated biochemistry, 30th Edition]



Conversion of arachidonic acid to prostaglandins and thromboxanes of series 2. (HHT, hydroxyheptadecatrienoate; PG, prostaglandin; PGI, prostacyclin; TX, thromboxane.) (*Both of these starred activities are attributed to the cyclooxgenase enzyme [prostaglandin H synthase]. Similar conversions occur in prostaglandins and thromboxanes of series 1 and 3.)

36. b) Cholesterol

Squalene can fold into a structure that closely resembles the steroid nucleus . Before ring closure occurs, squalene is converted to squalene 2,3-epoxide by a mixed-function oxidase in the endoplasmic reticulum, squalene epoxidase. The methyl group on C14 is transferred to C13 and that on C8 to C14 as cyclization occurs, catalyzed by oxidosqualene-lanosterol cyclase.

37. b) Linoleic acid

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Some polyunsaturated fatty acids cannot be synthesized by mammals & are nutritionally essential:

- Palmitoleic and oleic acids are not essential in the diet because the tissues can introduce a double bond at the Δ9 position of a saturated fatty acid.
- Linoleic and α-linolenic acids are the only fatty acids known to be essential for the complete nutrition of many species of animals, including humans, and are termed the nutritionally essential fatty acids.
- In most mammals, arachidonic acid can be formed from linoleic acid. Double bonds can be introduced at the Δ4, Δ5, Δ6, and Δ9 positions in most animals, but never beyond the Δ9 position.

Deficiency symptoms occur when the essential fatty acids are absent from the diet :

- Rats fed a purified nonlipid diet containing vitamins A and D exhibit a reduced growth rate and reproductive deficiency which may be cured by the addition of linoleic, α-linolenic, and arachidonic acids to the diet.
- These fatty acids are found in in high concentrations in vegetable oils and in small amounts in animal carcasses.
- Essential fatty acids are required for prostaglandin, thromboxane, leukotriene, and lipoxin formation and they also have various other functions that are less well defined.
- They are found in the structural lipids of the cell, often in the position 2 of phospholipids, and are concerned with the structural integrity of the mitochondrial membrane.
- Arachidonic acid is present in membranes and accounts for 5% to 15% of the fatty acids in phospholipids.
- Docosahexaenoic acid (DHA; ω3, 22:6), which is synthesized to a limited extent from α-linolenic acid or obtained directly from fish oils, is present in high concentrations in retina, cerebral cortex, testis, and sperm.

DHA is particularly needed for development of the brain and retina and is supplied via the placenta and milk.

- Patients with retinitis pigmentosa are reported to have low blood levels of DHA. In essential fatty acid deficiency, nonessential polyenoic acids of the ω9 family, particularly Δ5,8,11-eicosatrienoic acid (ω9 20:3) (Figure 23–10), replace the essential fatty acids in phospholipids, other complex lipids, and membranes. The triene:tetraene ratio in plasma lipids can be used to diagnose the extent of essential fatty acid deficiency.

38. b) Acetyl CoA enzyme

[Ref: Harper's Illustrated biochemistry, 30th Edition]

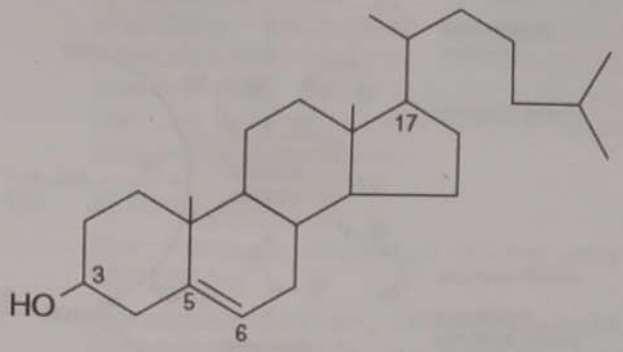
Regulation of acetyl CoA carboxylase. AcetylCoA carboxylase is activated by citrate, which promotes the conversion of the enzyme from an inactive dimer to an active polymeric form. Inactivation is promoted by phosphorylation of the enzyme and by long-chain acyl-CoA molecules such as palmitoyl

CoA. In addition, acyl-CoA inhibits the tricarboxylate transporter, which transports citrate out of mitochondria into the cytosol, thus decreasing the citrate concentration in the cytosol and favoring inactivation of the enzyme.

39. a) 27 carbon atoms

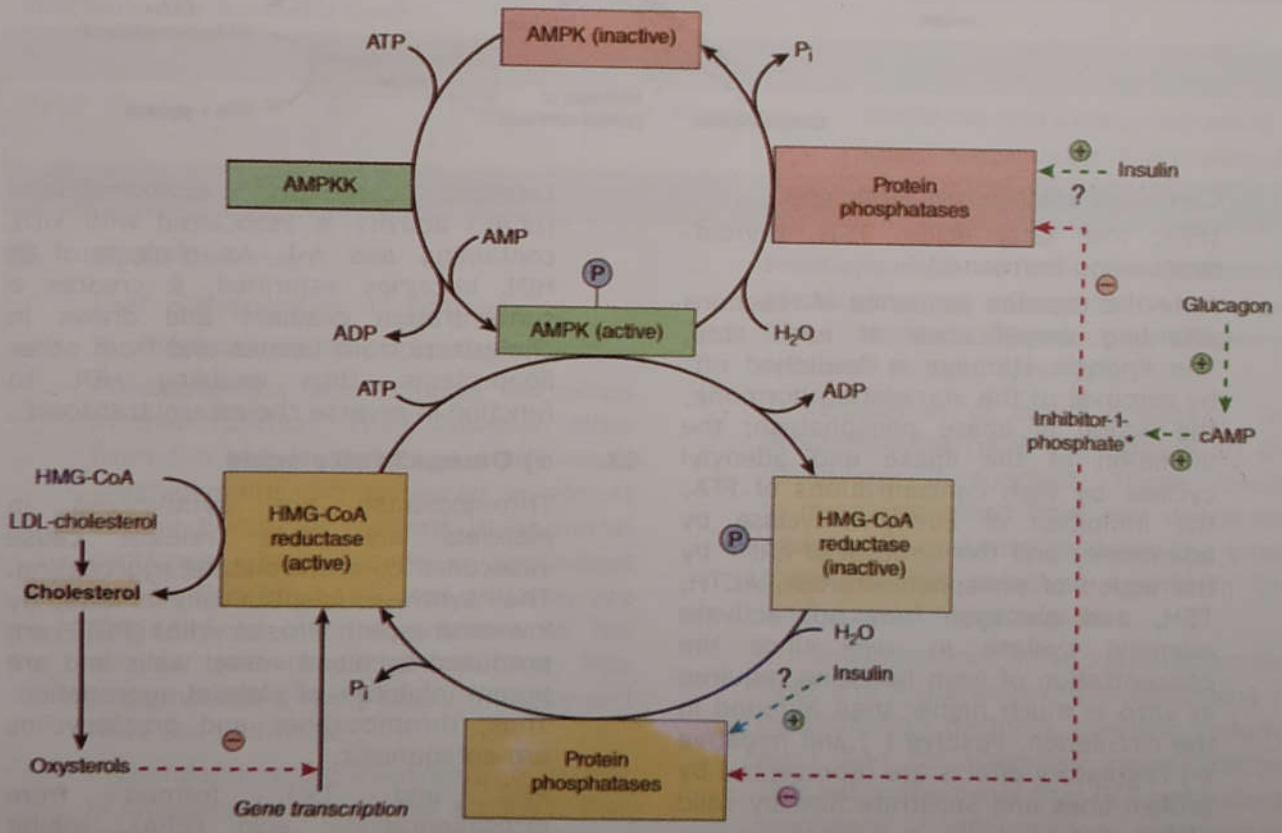
[Ref: Harper's Illustrated biochemistry, 30th Edition]

Cholesterol Is a Significant Constituent of Many Tissues Cholesterol is widely distributed in all cells of the body but particularly in nervous tissue. It is a major constituent of the plasma membrane and of plasma lipoproteins. It is often found as cholesteryl ester, where the hydroxyl group on position 3 is esterified with a long-chain fatty acid. It occurs in animals but not in plants or bacteria.



40. b) HMG CoA reductase

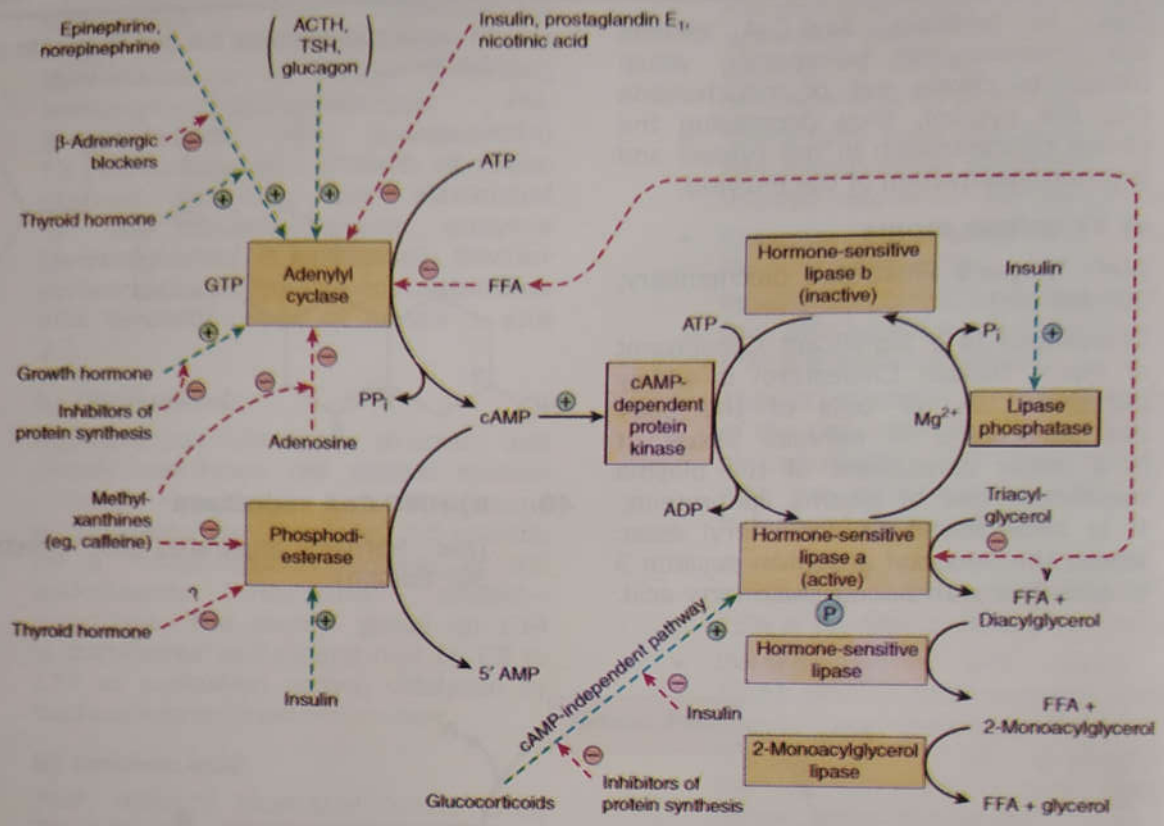
[Ref: Harper's Illustrated biochemistry, 30th Edition]



Cholesterol synthesis is controlled by regulation of hmg coa Reductase

41. a) Adrenaline

[Ref: Harper's Illustrated biochemistry, 30th Edition]



Control of adipose tissue lipolysis.

(FFA, free fatty acids; TSH, thyroid-stimulating hormone.)

Note the cascade sequence of reactions affording amplification at each step. The lipolytic stimulus is "switched off" by removal of the stimulating hormone; the action of lipase phosphatase; the inhibition of the lipase and adenylyl cyclase by high concentrations of FFA; the inhibition of adenylyl cyclase by adenosine; and the removal of cAMP by the action of phosphodiesterase. ACTH, TSH, and glucagon may not activate adenylyl cyclase in vivo since the concentration of each hormone required in vitro is much higher than is found in the circulation. Positive ( ) and negative (-) regulatory effects are represented by broken lines and substrate flow by solid lines.

42. c) Helps in the conversion of cholesterol ester

Plasma LCAT Is Responsible for Virtually All Plasma Cholesteryl Ester in Humans

Lecithin: cholesterol acyltransferase (LCAT) activity is associated with HDL containing apo A-I. As cholesterol in HDL becomes esterified, it creates a concentration gradient and draws in cholesterol from tissues and from other lipoproteins, thus enabling HDL to function in reverse cholesterol transport .

43. d) Omega3 fatty acids

Thromboxanes are synthesized in platelets and upon release cause vasoconstriction and platelet aggregation. Their synthesis is specifically inhibited by low-dose aspirin. Prostacyclins (PGI2) are produced by blood vessel walls and are potent inhibitors of platelet aggregation. Thus, thromboxanes and prostacyclins are antagonistic.

PG3 and TX3, formed from eicosapentaenoic acid (EPA), inhibit the release of arachidonate from phospholipids and the formation of PG2 and TX2.

PGI3 is as potent an antiaggregator of platelets as PGI2, but TXA3 is a weaker

aggregator than TXA2, changing the balance of activity and favoring longer clotting times. And hence omega 3 fatty acids which form PGI3 & TXA3 are cardioprotective.

Extra edge:

As little as 1 ng/ mL of plasma prostaglandins causes contraction of smooth muscle in animals. Potential therapeutic uses include prevention of conception, induction of labor at term, termination of pregnancy, prevention or alleviation of gastric ulcers, control of inflammation and of blood pressure, and relief of asthma and nasal congestion. In addition, PGD2 is a potent sleep-promoting substance. Prostaglandins increase cAMP in platelets, thyroid, corpus luteum, fetal bone, adenohypophysis, and lung but reduce cAMP in renal tubule cells and adipose tissue.

44. a) Oleic acid

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Monounsaturated (monoethenoid, monoenoic) acids, containing one double bond.

Number of C Atoms and Number and Position of Common Double Bonds	Family	Common Name	Systematic Name	Occurrence
Monoenolc acids (one double bond)				
16:1;9	ω7	Palmitolelc	c/s-9-Hexadecenoic	In nearly all fats
18:1;9	ω9	Oleic	c/s-9-Octadecenoic	Possibly the most common fatty acid in natural fats; particularly high In olive oil
16:1;9	ω9	Elaidic	Trans-9-Octadecenoic	Hydrogenated and ruminant fats

45. d) All the true

[Ref: Satyanarayan 4th Edition]

Biochemical actions of prostaglandins:

Prostaglandins act as local hormones in their function. They, however, differ from the true hormones in many ways. Prostaglandins are produced in almost all the tissues in contrast to hormonal synthesis which occurs in specialized glands. PGs are not stored and they are degraded to inactive products at the site of their production. Further, PGs are produced in very small amounts and have low half-lives.

Prostaglandins are involved in a variety of biological functions. The actions of PGs differ in different tissues. Sometimes, PGs bring about opposing actions in the same tissue.

Overproduction of PGs results in many symptoms which include pain, fever, nausea, vomiting and inflammation.

Prostaglandins mediate the regulation of blood pressure, inflammatory response, blood clotting, reproductive functions, response to pain, fever etc.

1. Regulation of blood pressure: The prostaglandins (PGE, PGA and PCI2) are vasodilator in function. These results in increased blood flow and decreased peripheral resistance to lower the blood pressure. PGs serve as agents in the treatment of hypertension.

2. Inflammation: The prostaglandins PGEl and PGE2 induce the symptoms of inflammation (redness, swelling, edema etc.) due to arteriolar vasodilatation. This led to the belief that PCs are natural mediators of inflammatory reactions of rheumatoid arthritis (involving joints), psoriasis (skin), conjunctivitis (eyes) etc. Corticosteroids are frequently used to treat these inflammatory reactions, since they inhibit prostaglandin synthesis.

3. Reproduction: Prostaglandins have

widespread applications in the field of reproduction. PGE2 and PGF2 are used for the medical termination of pregnancy and induction of Iabor. Prostaglandins are administered to cattle to induce estrus and achieve better rate of fertilization.

4. Pain and fever: It is believed that pyrogens (fever producing agents) promote prostaglandin biosynthesis leading to the formation of PGE2 in the hypothalamus, the site of regulation of body temperature. PGE2 along with histamine and bradykinin cause pain. Migraine is also due to PGE2. Aspirin and other non-steroidal drugs inhibit PG synthesis and thus control fever and relieve pain.

5. Regulation of gastric secretion : In general, prostaglandins (PGE) inhibit gastric secretion. PGs are used for the treatment of gastric ulcers. However, PGs stimulate pancreatic secretion and increase the motility of intestine which often causes diarrhea.

6. Influence on immune system in Macrophages secrete PGE which decreases the immunological functions of B-and T-lymphocytes.

7. Effects on respiratory function : PGE is a bronchodilator whereas PGF acts as a constrictor of bronchial smooth muscles. Thus, PGE and PGF oppose the actions of each other in the lungs. PGEI and PGE2 are used in the treatment of asthma.

8. Influence on renal functions: ECF increases glomerular filtration rate (GFR) and promotes urine output. Excretion of Na+ and K+ is also increased by PGE.

9. Effects on metabolism: Prostaglandins influence certain metabolic reactions, probably through the mediation of cAMP. PGE decreases lipolysis, increases glycogen formation and promotes calcium mobilization from the bone.

10. Platelet aggregation and thrombosis: The prostaglandins, namely prostacyclins (PGI2), inhihit platelet aggregation. On the other hand, thromboxanes (TXA2) and prostaglandin E2 promote platelet aggregation and blood clotting that might lead to thrombosis. PGI2, produced by endothelial cells lining the blood vessels, prevents the adherence of platelets to the blood vessels. TXA2 is released by the platelets and is responsible for their spontaneous aggregation when the platelets come in contact with foreign surface, collagen or thrombin. Thus, prostacyclins and thromboxanes are antagonists in their action. In the overall effect PCI2 acts as a vasodilator, while TXA2 is a vasoconstrictor. The balance between PCI2 and TXA2 is important in the regulation of hemostasis and thrombosis.

46. d) Cervonic acid

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Saturated Fatty Acids

Common Name	Number of C Atoms	Occurrence
Acetic	2	Major end product of carbohydrate fermentation by rumen organisms
Butyric	4	In certain fats in small amounts (especially butter). An end product of carbohydrate fermentation by rumen organisms3.
Valeric	5	
Caproic	6	
Laurie	12	Spermaceti, cinnamon, palm kernel, coconut oils, laurels, butter.
Myristic	14	Nutmeg, palm kernel, coconut oils, myrtles, butter.
Palmitic	16	Common in all animal and plant fats.
Stearic	18	

Unsaturated Fatty Acids of Physiologic and Nutritional Significance

Number of C Atoms and Number and Position of Common Double Bonds	Family	Common Name	Systematic Name	Occurrence
Monoenoic acids (one double bond)				
16:1;9	ω7	Palmitolelc	c/s-9-Hexadecenoic	In nearly all fats.
18:1;9	ω9	Oleic	c/s-9-Octadecenoic	Possibly the most common fatty acid in natural fats; particularly high In olive oil.
16:1;9	ω9	Elaidic	Trans-9-Octadecenoic	Hydrogenated and ruminant fats.
Dienoic acids (two double bonds)				
18:2;9,12	ω6	linoleic	all - cis - 9, 12 Octadecadienoic	Corn, peanut, cottonseed, soy bean and many plant oils.
Trienoic acids (three double bonds)				
18:3;6,9,12	ω6	γ - Linolenic	all - cis- 6, 9, 12 Octadecatrienoic	Some plants, eg, oil of evening primrose, borage oil; minor fatty acid in animals.
18: 3; 6, 9, 12	ω3	α - Linolenic	all - cis - 9, 12, 15 - Octadecatrienoic	Frequently found with linoleic acid but particularly in linseed oil.
Tetraenoic acids (four double bonds)				
20: 4; 5, 8, 11, 14	ω6	Arachidonic	all - cis - 5, 8, 11, 14 - Eicosatetraenoic	Found in animal fats; important component of phospholipids in animals.
Pentaenoic acids (five double bonds)				
20: 5; 5, 8, 11, 14, 17	ω3	Timnodonic	all - cis - 5, 8, 11, 14, 17 - Eicosapentaenoic	Important component of fish oils, eg, cod liver, mackerel, salmon oils.
Hexaenoic acids (six double bonds)				
22: 6; 4, 7, 10, 13, 16, 19	ω3	Cervonic	all - cis - 4, 7, 10, 13, 16, 19 - Docosahexaenoic	Fish oils, algal oils, phospholipids in brain.

47. b) Cardiolipin

Cardiolipin

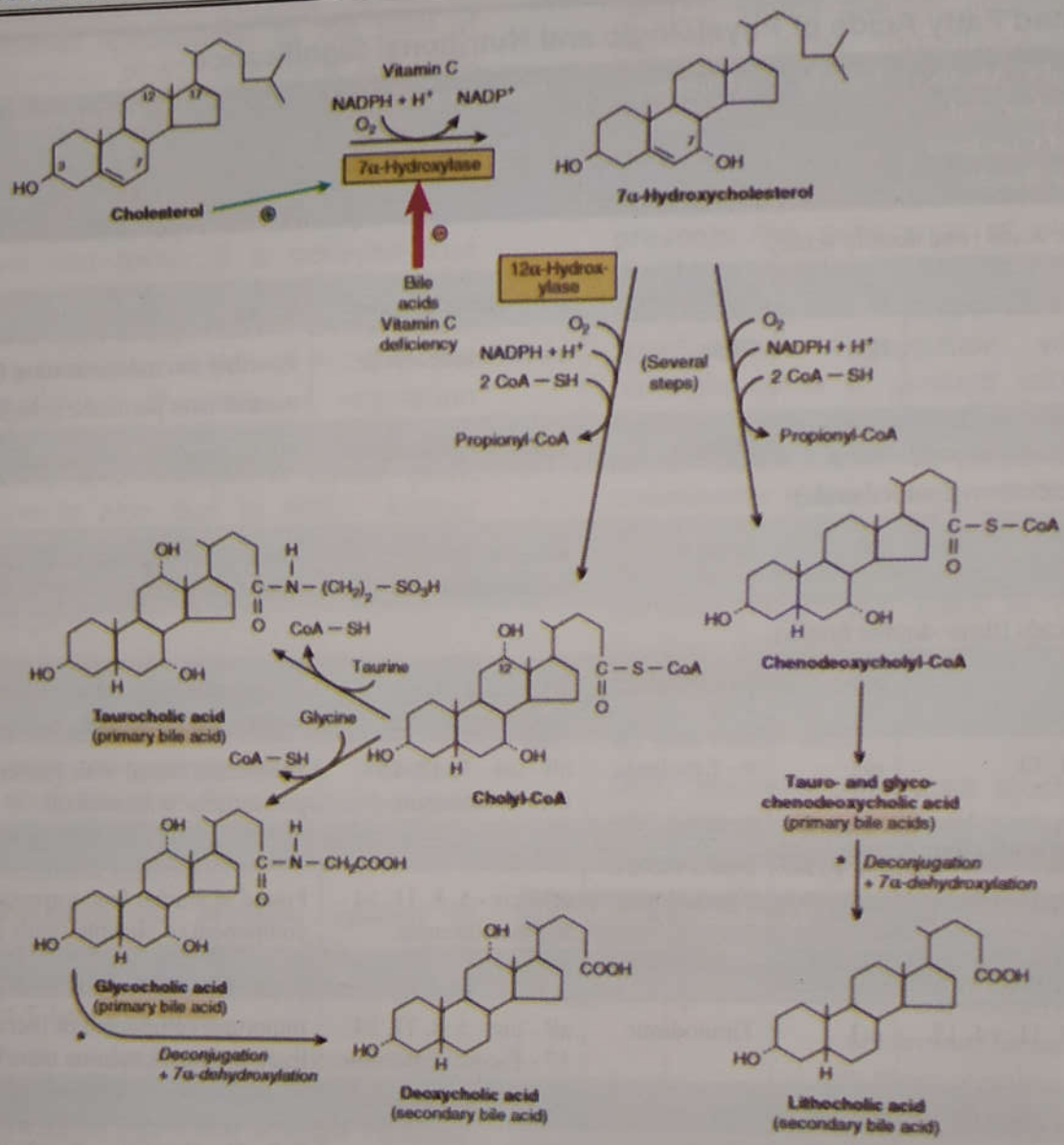
Is a Major Lipid of Mitochondrial Membranes Phosphatidic acid is a precursor of phosphatidylglycerol, which in turn gives rise to cardiolipin. This phospholipid is found only in mitochondria and is essential for the mitochondrial function. Decreased cardiolipin levels or alterations in its structure or metabolism cause mitochondrial dysfunction in aging and in pathological conditions including heart failure, hypothyroidism, and Barth syndrome (cardioskeletal myopathy).

Cardiolipin (diphosphatidylglycerol) is a phospholipid present in mitochondria. It is formed from phosphatidylglycerol, which in turn is synthesized from CDPdiacylglycerol and glycerol 3-phosphate. Cardiolipin, found in the inner membrane of mitochondria, has a key role in mitochondrial structure and function, and is also thought to be involved in programmed cell death (apoptosis).

48. c) Chenodeoxycnolic acid

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Bile Acids Are Formed from Cholesterol The primary bile acids are synthesized in the liver from cholesterol. These are cholic acid (found in the largest amount in most mammals) and chenodeoxycholic acid.



49. c) Triglyceride

Adipose tissue triacylglycerol is the main fuel reserve of the body. It is hydrolyzed (lipolysis) and glycerol and nonesterified (free) fatty acids are released into the circulation.

50. b) PUFA

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Lipid peroxidation is a source of free radicals

Peroxidation (auto-oxidation) of lipids exposed to oxygen is responsible not only for deterioration of foods (rancidity), but also for damage to tissues in vivo, where it may be a cause of cancer, inflammatory diseases, atherosclerosis, and aging. The deleterious effects are considered to be caused by free radicals, molecules that have unpaired valence electrons, making them highly reactive. Free radicals containing oxygen (eg, ROOt, ROt, OHt) are termed reactive oxygen species (ROS). These are produced during peroxide formation from fatty acids containing methylene-interrupted double bonds, that is, those found in the naturally occurring polyunsaturated fatty acids.Lipid peroxidation is a chain reaction providing a continuous supply of ROS that initiate further peroxidation and thus has potentially devastating effects. The whole process can be depicted as follows:

1. Initiation:

$$ROOH + Metal^{(n)+} \rightarrow ROO^{\cdot} + Metal^{(n-1)+} + H^{+}$$

$$X^{\cdot} + RH \rightarrow R^{\cdot} + XH$$

2. Propagation:

$$R^{\cdot} + O_2 \rightarrow ROO^{\cdot}$$

$$ROO^{\cdot} + RH \rightarrow ROOH + R^{\cdot}, \text{etc}$$

3. Termination:

$$ROO^{\cdot} + ROO^{\cdot} \rightarrow ROOR + O_2$$

$$ROO^{\cdot} + R^{\cdot} \rightarrow ROOR$$

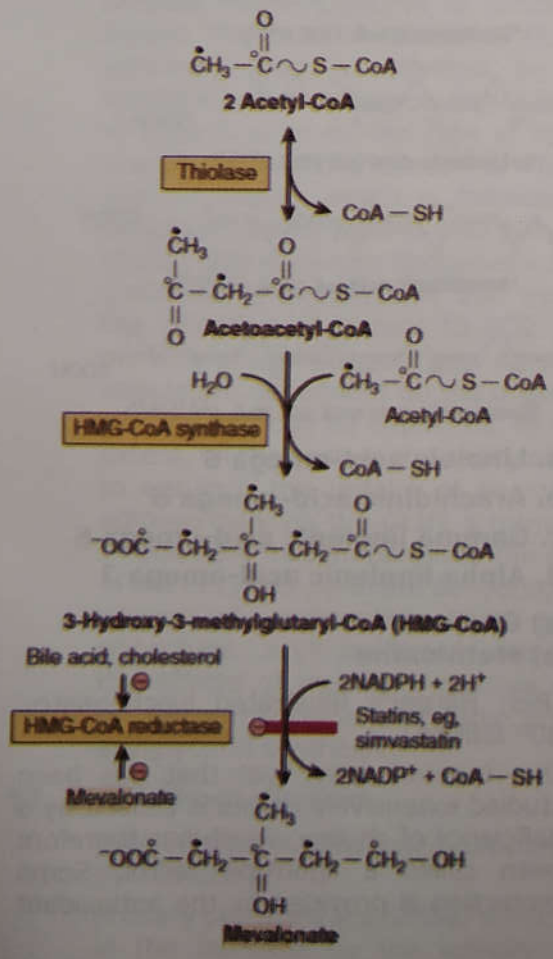
$$R^{\cdot} + R^{\cdot} \rightarrow RR$$

51. d) 3-hydroxy-3-methyglutaryl CoA

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Biosynthesis of mevalonate:

HMG-CoA reductase is inhibited by statins. The open and solid circles indicate the fate of each of the carbons in the acetyl moiety of acetyl-CoA.



52. a) Glycerol

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Gangliosides are complex glycosphingolipids derived from glucosylceramide that contain in addition one or more molecules of a sialic acid. Neuraminic acid (NeuAc) is the principal sialic acid found in human tissues. Gangliosides are also present in nervous tissues in high concentration. They function in cell-cell recognition and communication and as receptors for hormones and bacterial toxins such as cholera toxin. The simplest ganglioside found in tissues is GM3, which contains ceramide, one molecule of glucose, one molecule of galactose, and one molecule of NeuAc. In the shorthand nomenclature used, G represents ganglioside; M is a monosialo-containing species; and the subscript 3 is a number assigned on the basis of chromatographic migration. GM1, a more complex ganglioside derived from GM3, is of considerable biologic interest, as it is known to be the receptor in human intestine for cholera toxin.

53. c) Plasma albumin

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Free fatty acids are rapidly metabolized

The FFAs (also termed nonesterified fatty acids [NEFAs] or unesterified fatty acids) arise in the plasma from the breakdown of triacylglycerol in adipose tissue or as a result of the action of lipoprotein lipase on the plasma triacylglycerols. They are found in combination with albumin, a very effective solubilizer, in concentrations varying between 0.1 and 2.0 μeq/mL of plasma. Levels are low in the fully fed condition and rise to 0.7 to 0.8 μeq/mL in the starved state. In uncontrolled diabetes mellitus, the level may rise to as much as 2 μeq/mL. FFAs are removed from the blood extremely rapidly and oxidized (fulfilling 25%-50% of energy requirements in starvation) or esterified to form triacylglycerol in the tissues. In starvation, esterified lipids from the circulation or in the tissues are oxidized as well, particularly in heart and skeletal muscle cells, where considerable

stores of lipid are to be found. The FFA uptake by tissues is related directly to the plasmaFFA concentration, which in turn is determined by the rate of lipolysis in adipose tissue. After dissociation of the fatty acidalbumin compiex at the plasma membrane, fatty acids bind to a membrane fatty acid transport protein that acts as a transmembrane cotransporter with Na+. On entering the cytosol, FFAs are bound by intracellular fatty-acid-binding proteins. The role of these proteins in intracellular transport is thought to be similar to that of serum albumin in extracellular transport of long-chain fatty acids.

54. b) Enzyme Glycerol kinase plays an important role

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Biosynthesis of triacylglycerol :

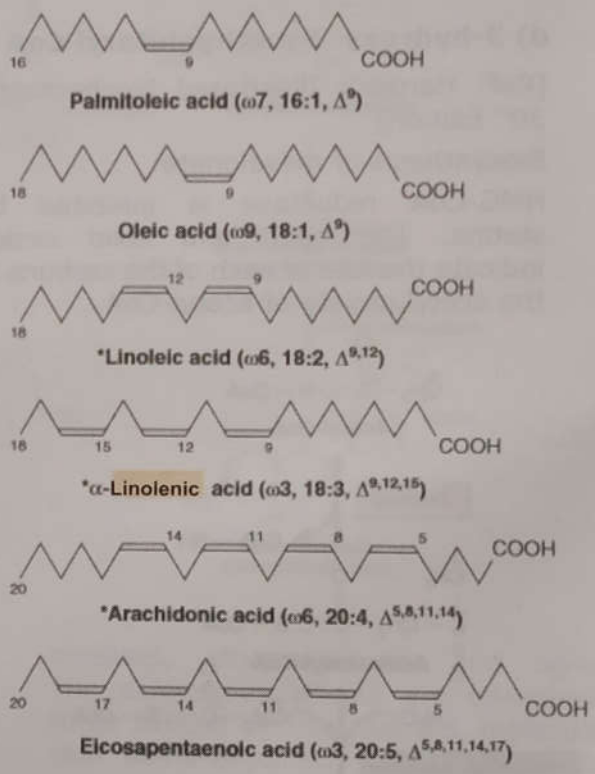
Two molecules of acyl-CoA, formed by the activation of fatty acids by acyl-CoA synthetase, combine with glycerol-3-phosphate to form phosphatidate (1,2-diacylglycerol phosphate). This takes place in two stages, catalyzed by glycerol-3-phosphate acyltransferase and 1-acylglycerol3-phosphate acyltrans ferase. Phosphatidate is converted by phosphatidate phosphohydrolase (also called phosphatidate phosphatase (PAP)) and diacylglycerol acyltransferase (DGAT) to 1,2-diacylglycerol and then triacylglycerol. Lipins, a family of three proteins, have PAP activity and they also act as transcription factors which regulate the expression of genes involved in lipid metabolism. DGAT catalyzes the only step specific for triacylglycerol synthesis and is thought to be rate limiting in most circumstances. In intestinal mucosa, monoacylglycerol acyltransferase converts monoacy-lglycerol to 1,2-diacylglycerol in the monoacylglycerol pathway. Most of the activity of these enzymes resides in the endoplasmic reticulum, but some is found in mitochondria. Although phosphatidate phosphohydrolase protein is found mainly in the cytosol, the active form of the enzyme is membrane bound.

55. a) Acetyl CoA

The main pathway for de novo synthesis of fatty acids lipogenesis occurs in the cytosol

This system is present in many tissues, including liver, kidney, brain, lung, mammary gland, and adipose tissue. Its cofactor requirements include NADPH, ATP, Mn2+, biotin, and HCO3− (as a source of CO2). Acetyl-CoA is the immediate substrate, and free palmitate is the end product.

56. d) Alpha linolenic acid



a. Linoleic acid-omega 6
b. Arachidinic acid-omega 6
c. Gamma linolenic acid-omega 6
d. Alpha linolenic acid-omega 3

57. a) Choline
b) Methionine

[Ref: Harper's Illustrated biochemistry, 30th Edition]

One type of fatty liver that has been studied extensively in rats is caused by a deficiency of choline, which has therefore been called a lipotropic factor. Some protection is provided by the antioxidant

action of vitamin E-supplemented diets. The action of ethionine is thought to be caused by a reduction in availability of ATP due to its replacing methionine in S-adenosylmethionine, trapping available adenine and preventing synthesis of ATP. Orotic acid also causes fatty liver; it is believed to interfere with glycosylation of the lipoprotein, thus inhibiting release, and may also impair the recruitment of triacylglycerol to the particles. A deficiency of vitamin E enhances the hepatic necrosis of the choline deficiency type of fatty liver. Added vitamin E or a source of selenium has a protective effect by combating lipid peroxidation. In addition to protein deficiency, essential fatty acid and vitamin deficiencies (eg, linoleic acid, pyridoxine, and pantothenic acid) can cause fatty infiltration of the liver.

58. a) Insulin

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Hormones regulate fat mobilization

Adipose Tissue Lipolysis Is Inhibited by Insulin The rate of release of FFA from adipose tissue is affected by many hormones that influence either the rate of esterification or the rate of lipolysis. Insulin inhibits the release of FFA from adipose tissue, which is followed by a fall in circulating plasma free fatty acids. Insulin also enhances lipogenesis and the synthesis of acylglycerol and increases the oxidation of glucose to CO2 via the pentose phosphate pathway. All of these effects are dependent on the presence of glucose and can be explained, to a large extent, on the basis of the ability of insulin to enhance the uptake of glucose into adipose cells via the GLUT 4 transporter. In addition, insulin increases the activity of the enzymes pyruvate dehydrogenase, acetyl-CoA carboxylase, and glycerol phosphate acyltransferase, reinforcing the effects of increased glucose uptake on the enhancement of fatty acid and acylglycerol synthesis.

59. c) Lithocholic acid

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Primary bile acids are further metabolized in the intestine by the activity of the intestinal bacteria. Thus, deconjugation and 7α-dehydroxylation occur, producing the secondary bile acids, deoxycholic acid, and lithocholic acid.

Most Bile Acids Return to the Liver in the Enterohepatic Circulation Although products of fat digestion, including cholesterol, are absorbed in the first 100 cm of small intestine, the primary and secondary bile acids are absorbed almost exclusively in the ileum, and 98% to 99% is returned to the liver via the portal circulation. This is known as the enterohepatic circulation . However, lithocholic acid, because of its insolubility, is not reabsorbed to any significant extent. Only a small fraction of the bile salts escapes absorption and is therefore eliminated in the feces. Nonetheless, this represents a major pathway for the elimination of cholesterol. Each day the pool of bile acids (about 3-5 g) is cycled through the intestine 6 to 10 times and an amount of bile acid equivalent to that lost in the feces is synthesized from cholesterol, so that a pool of bile acids of constant size is maintained. This is accomplished by a system of feedback controls.

60. b) Transport of fatty acids from cytosol to mitochondria

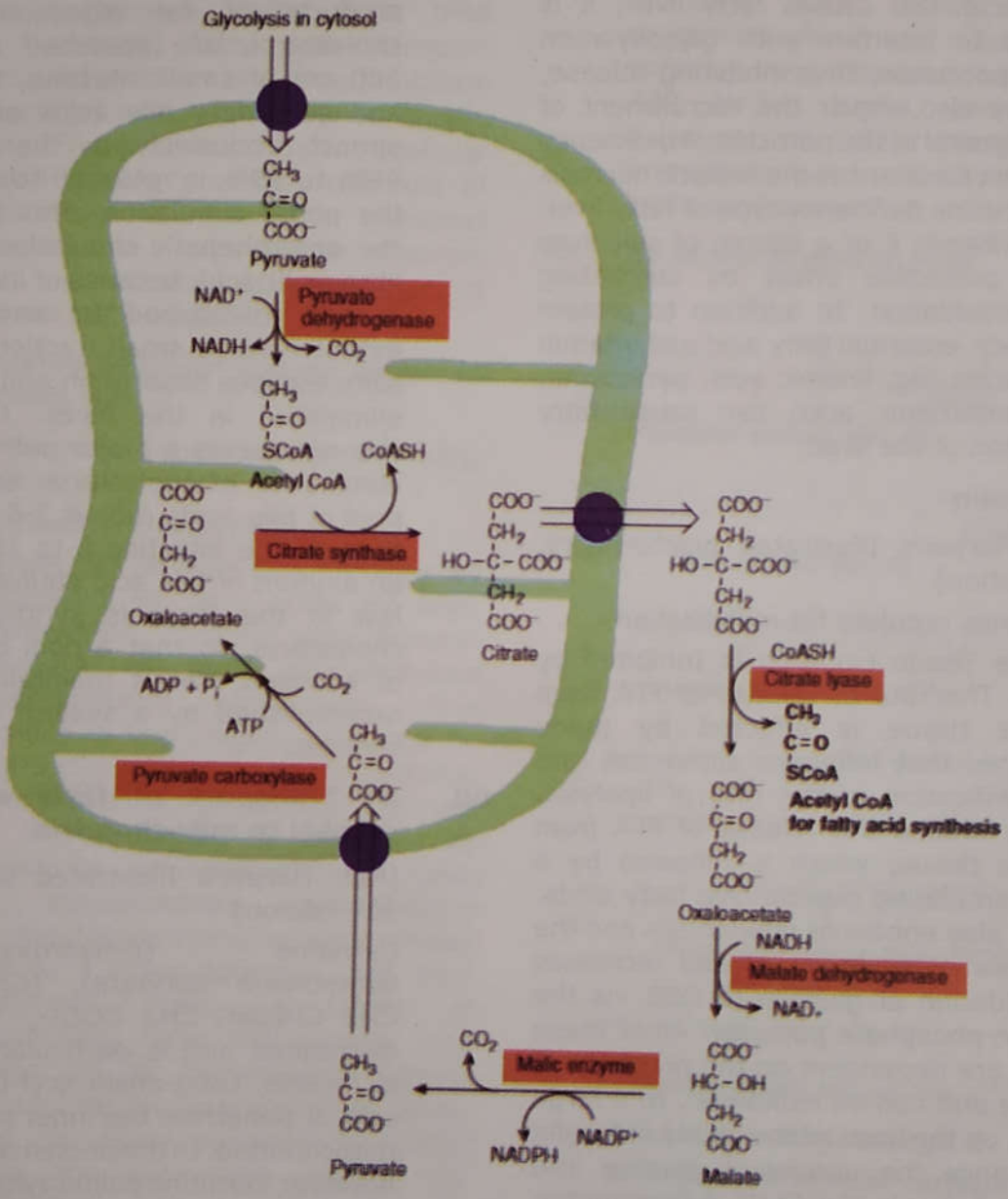
[Ref: Harper's Illustrated biochemistry, 30th Edition]

Carnitine (β-hydroxy-γ-trimethy-lammonium butyrate), (CH3)3 N +´ CH2´CH(OH)´CH2´COO−, is widely distributed and is particularly abundant in muscle. Long-chain acyl-CoA (or FFA) cannot penetrate the inner membrane of mitochondria. In the presence of carnitine, however, carnitine palmitoyltransferase-I, located in the outer mitochondrial membrane, transfers long-chain acyl group from CoA to carnitine, forming acylcarnitine and releasing CoA. Acylcarnitine is able to penetrate the inner membrane and gain access to the β-oxidation system of enzymes via the inner membrane exchange transporter carnitine-acylcarnitine translocase. The transporter binds acylcarnitine and transports it across the membrane in exchange for carnitine. The acyl group is then transferred to CoA so that acyl-CoA is reformed and carnitine is liberated.

This reaction is catalyzed by carnitine palmitoyltransferase-II, which is located on the inside of the inner membrane.

61. b) ATP citrate lyase

[Ref: Harper's Illustrated biochemistry, 30th Edition]



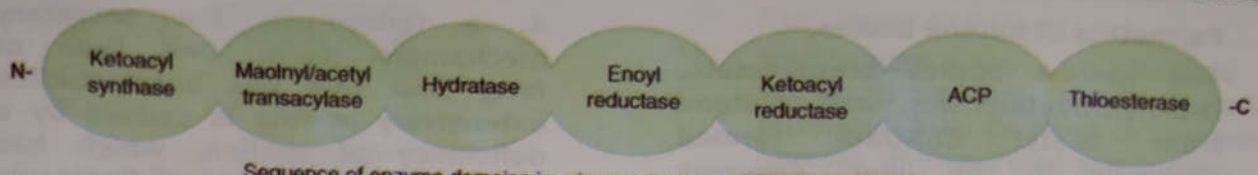
62. c) 7-alpha hydroxylase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

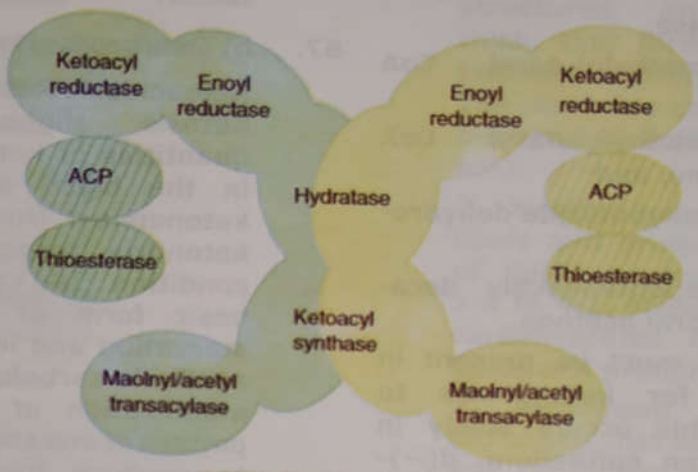
The 7α-hydroxylation of cholesterol degradation is the first and principal regulatory step in the biosynthesis of bile acids and is catalyzed by cholesterol 7`-hydroxylase, a microsomal cytochrome P450 enzyme designated CYP7A1. A typical monooxygenase, it requires oxygen, NADPH, and cytochrome P450.

63. c) Acetyl Co A carboxylase

[Ref: Harper's Illustrated biochemistry, 30th Edition]



Sequence of enzyme domains in primary structure of fatty acid synthase monomer



Fatty acid synthase homodimer

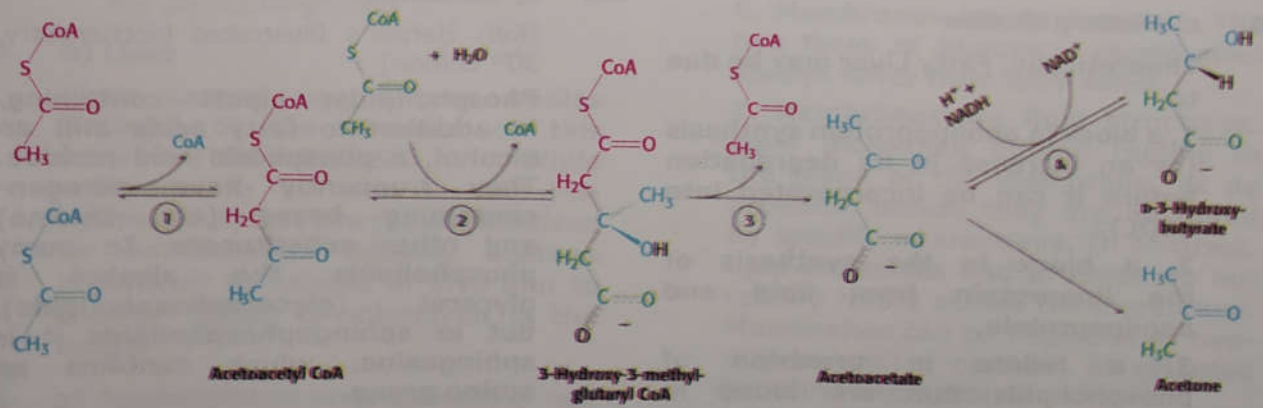
Fatty acid synthase multienzyme complex. The complex is a dimer of two identical polypeptide monomers in which six enzymes and the acyl carrier protein (ACP) are linked in the primary structure in the sequence shown. X-ray crystallography of the three-dimensional structure has demonstrated that the two monomers in the complex are arranged in an X-shape. The position of the ACP and thioesterase is not yet resolved, but they are thought to be close to the 3 ketoacyl reductase enzyme domain.

64. c) Miochondria

[Ref: Stryer 8th Edition]

Ketogenesis occurs in liver mitochondria:

The ratio of hydroxybutyrate to acetoacetate depends on the NADH/ NAD1 ratio inside mitochondria. Because it is a b-ketoacid, acetoacetate also undergoes a slow, spontaneous decarboxylation to acetone. The odor of acetone may be detected in the breath of a person who has a high level of acetoacetate in the blood.



Formation of ketone bodies.

The ketone bodies—acetoacetate, D-3-hydroxybutyrate, and acetone from acetyl CoAOare formed primarily in the liver. Enzymes catalyzing these reactions are

(1) 3-ketothiolase,

(2) hydroxymethylglutaryl CoA synthase,

(3) hydroxymethylglutaryl CoA cleavage enzyme, and

(4) D - 3 - hydroxybutyrate dehydrogenase.

Acetoacetate spontaneously decarboxylates to form acetone.

Both enzymes must be present in mitochondria for ketogenesis to take place. This occurs solely in liver and rumen epithelium. d(−)-3-Hydroxybutyrate is quantitatively the predominant ketone body present in the blood and urine in ketosis.

65. d) Coconut oil

Consumption of PUFA: Dietary intake of pofyunsaturated fatty acids (PUFA) reduces the plasma cholesterol level. PUFA will help in transport of cholesterol by LCAT mechanism and its excretion from the body. The oils with rich PUFA content include cottonseed oil, soya bean oil, sunflower oil, corn oil, fish oils etc. ghee and coconut oil are poor sources of PUFA.

66. c) Dietary choline

Theoretically, Fatty Liver may be due to

1. a block in apolipoprotein synthesis (or an increase in its degradation before it can be incorporated into VLDL),

2. a block in the synthesis of the lipoprotein from lipid and apolipoprotein,

3. a failure in provision of phospholipids that are found in lipoproteins, or

4. a failure in the secretory mechanism itself. One type of fatty liver that has been studied extensively in rats is caused by a deficiency of choline, which has therefore been called a lipotropic factor.

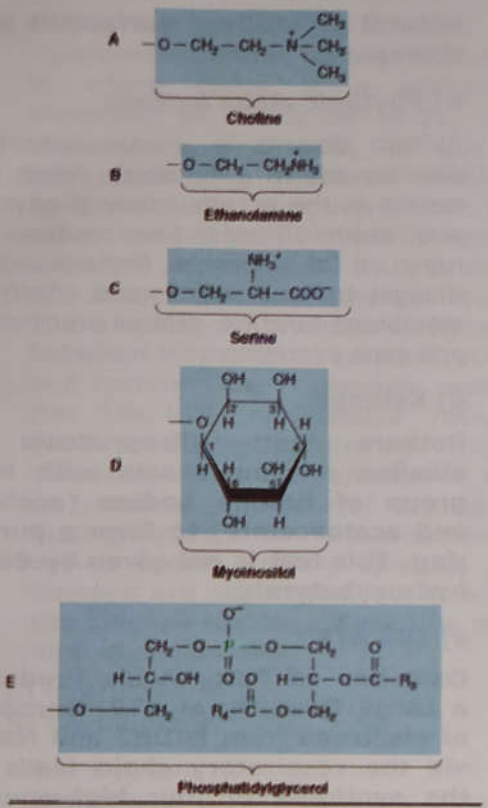
67. b) Overproduction of acetyl CoA

Ketoacidosis Results From Prolonged Ketosis Higher than normal quantities of ketone bodies present in the blood or urine constitute ketonemia (hyperketonemia) or ketonuria, respectively. The overall condition is called ketosis. The basic form of ketosis occurs in starvation and involves depletion of available carbohydrate coupled with mobilization of FFA. This general pattern of metabolism is exaggerated to produce the pathologic states found in diabetes mellitus, the type 2 form of which is increasingly common in Western countries; twin lamb disease; and ketosis in lactating cattle. Nonpathologic forms of ketosis are found under conditions of high-fat feeding and after severe exercise in the postabsorptive state. Acetoacetic and 3-hydroxybutyric acids are both moderately strong acids and are buffered when present in blood or other tissues. However, their continual excretion in quantity progressively depletes the alkali reserve, causing ketoacidosis. This may be fatal in uncontrolled diabetes mellitus.

68. c) Ceramide

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Phospholipids: Lipids containing, in addition to fatty acids and an alcohol, a phosphoric acid residue. They frequently have nitrogen-containing bases (eg, choline) and other substituents. In many phospholipids the alcohol is glycerol (glycerophospholipids), but in sphingophospholipids it is sphingosine, which contains an amino group.



Phospholipids. The O— shown shaded in phosphatidic acid is substituted by the substituents shown to form the phospholipids: (A) 3-phosphatidylcholine, (B) 3-phosphatidylethanolamine, (C) 3-phosphatidylserine, (D) 3-phosphatidylinositol, and (E) cardiolipin (diphosphatidylglycerol).

- Ceramide: The combination of sphingosine plus fatty acid is known as ceramide, a structure also found in the glycosphingolipids

69. b) Liver

Liver cannot use ketone bodies because of the absence of this enzyme-THIOPHORASE. While acetoacetate and d(−)-3-hydroxybutyrate are readily oxidized by extrahepatic tissues, acetone is difficult to oxidize in vivo and to a large extent is volatilized in the lungs.

70. a) Asymmetrical arrangement of cell wall component

[Ref: Stryer 8th Edition]

Membranes are as diverse in structure as they are in function. However, they do have in common a number of important attributes:

1. Membranes are sheetlike structures, only two molecules thick, that form closed boundaries between different compartments. The thickness of most membranes is between 60 Å (6 nm) and 100 Å (10 nm).

2. Membranes consist mainly of lipids and proteins. The mass ratio of lipids to proteins ranges from 1:4 to 4:1. Membranes also contain carbohydrates that are linked to lipids and proteins.

3. Membrane lipids are small molecules that have both hydrophilic and hydrophobic moieties. These lipids spontaneously form closed bimolecular sheets in aqueous media. These lipid bilayers are barriers to the flow of polar molecules.

4. Specific proteins mediate distinctive functions of membranes. Proteins serve as pumps, channels, receptors, energy transducers, and enzymes. Membrane proteins are embedded in lipid bilayers, which create suitable environments for their action.

5. Membranes are noncovalent assemblies. The constituent protein and lipid molecules are held together by many noncovalent interactions, which act cooperatively.

6. Membranes are asymmetric. The two faces of biological membranes always differ from each other.

7. Membranes are fluid structures. Lipid molecules diffuse rapidly in the plane of the membrane, as do proteins, unless they are anchored by specific interactions. In contrast, lipid molecules and proteins do not readily rotate across the membrane. Membranes can be regarded as two-dimensional s olutions of oriented proteins and lipids.

8. Most cell membranes are electrically polarized, such that the

inside is negative [typically 260 millivolts (mV)]. Membrane potential plays a key role in transport, energy conversion, and excitability .

71. b) H2O2 formed

Peroxisomes Oxidize Very Long Chain Fatty Acids

A modified form of β-oxidation is found in peroxisomes and leads to the formation of acetyl-CoA and H_2O_2 (from the flavoprotein-linked dehydrogenase step), which is broken down by catalase. Thus, the dehydrogenation in peroxisomes is not linked directly to phosphorylation and the generation of ATP. The system facilitates the oxidation of very long chain fatty acids (eg, C20, C22). The enzymes responsible are induced by high-fat diets and in some species by hypolipidemic drugs such as clofibrate. The enzymes in peroxisomes do not attack shorter chain fatty acids; the β-oxidation sequence ends at octanoyl-CoA. Octanoyl and acetyl groups are both further oxidized in mitochondria. Another role of peroxisomal β-oxidation is to shorten the side chain of cholesterol in bile acid formation . Peroxisomes also take part in the synthesis of ether glycerolipids, cholesterol, and dolichol.

72. a) Dipalmitoyl phosphatidylcholine

Deficiency of Lung Surfactant Causes Respiratory Distress Syndrome

Lung surfactant is composed mainly of lipid with some proteins and carbohydrate and prevents the alveoli from collapsing. The phospholipid dipalmitoyl-phosphatidylcholine decreases surface tension at the air-liquid interface and thus greatly reduces the work of breathing, but other surfactant lipid and protein components are also important in surfactant function. Deficiency of lung surfactant in the lungs of many preterm newborns gives rise to infant respiratory distress syndrome (IRDS). Administration of either natural or artificial surfactant is of therapeutic benefit.

73. d) Phytanic alpha oxidase

Refsum disease is a rare neurologic disorder due to a metabolic defect that results in the accumulation of phytanic acid, which is found in dairy products and ruminant fat and meat. Phytanic acid is thought to have pathological effects on membrane function, protein prenylation, and gene expression.

74. d) Ketones

Rothera test: Nitroprusside in alkaline medium reacts with keto group of ketone bodies (acetone and acetoacetate) to form a purple ring. This test is not given by Beta-hydroxybutyrate.

75. a) 106 ATP

Oxidation of Fatty Acids Produces a Large Quantity of ATP Transport of electrons from $FADH_2$ and NADH via the respiratory chain leads to the synthesis of four high-energy phosphates (see Chapter 13) for each of the seven cycles needed for the breakdown of the C16 fatty acid, palmitate, to acetyl-CoA ($7 \times 4 = 28$). A total of 8 mol of acetyl-CoA is formed, and each gives rise to 10 mol of ATP on oxidation in the citric acid cycle, making $8 \times 10 = 80$ mol. Two must be subtracted for the initial activation of the fatty acid, yielding a net gain of 106 mol of ATP per mole of palmitate or $106 \times 30.5^{*} = 3233$ kJ. This represents 33% of the free energy of combustion of palmitic acid.

76. c) <3.5

Atherosclerosis is an inflammatory disease characterized by the deposition of cholesterol and cholesteryl ester from the plasma lipoproteins into the artery wall and is a major cause of heart disease. Elevated plasma cholesterol levels (>5.2 mmol/L) are one of the most important factors in promoting atherosclerosis, but it is now recognized that elevated

blood triacylglycerol is also an independent risk factor. Diseases in which there is a prolonged elevation of levels of VLDL, IDL, chylomicron remnants, or LDL in the blood (eg, diabetes mellitus, lipid nephrosis, hypothyroidism, and other conditions of hyperlipidemia) are often accompanied by premature or more severe atherosclerosis. There is also an inverse relationship between HDL (HDL2) concentrations and coronary heart disease, making the LDL:HDL cholesterol ratio a good predictive parameter. This is consistent with the function of HDL in reverse cholesterol transport. Susceptibility to atherosclerosis varies widely among species, and humans are one of the few in which the disease can be induced by diets high in cholesterol.

77. b) VLDL
d) Chylomicron

Triacylglycerol is transported from the intestines in chylomicrons and from the liver in very low density lipoproteins.

78. c) Apoprotein C-II lipoprotein lipase inhibitors

Apolipoproteins carry out several roles:

(1) they can form part of the structure of the lipoprotein, for example, apo B;

(2) they are enzyme cofactors, for example, C-II for lipoprotein lipase, A-I for lecithin:cholesterol acyltransferase, or enzyme inhibitors, for example, apo A-II and apo C-III for lipoprotein lipase, apo C-I for cholesteryl ester transfer protein;

(3) they act as ligands for interaction with lipoprotein receptors in tissues, for example, apo B-100 and apo E for the LDL receptor, apo E for the LDL-receptor-related protein-1 (LRP-1), which has been identified as the remnant receptor, and apo A-I for the HDL receptor.

The functions of apo A-IV and apo D, however, are not yet clearly defined, although apo D is believed to be an important factor in human neurodegenerative disorders.

79. a) APO B 100

[Ref: Stryer 8th Edition]

Apolipoproteins (apoproteins)

The protein cornponents of lipoproteins are known as apolipoproteins or simply, apoproteins. They perform the following functions

1. Act as structural components of lipoproteins.
2. Recognize the cell membrane surface receptors.
3. Activate enzymes involved in lipoprotein metabolism.

Plasma lipoproteins	Density (g ml^{-1})	Diameter (nm)	Apolipoprotein	Physiological role	Composition (%)				
					TAG	CE	C	PL	P
Chylomicron	<0.95	75–1200	B-48, C, E	Dietary fat transport	86	3	1	8	2
Very low density lipoprotein	0.95–1.006	30–80	B-100, C, E	Endogenous fat transport	52	14	7	18	8
Intermediate-density lipoprotein	1.006–1.019	15–35	B-100, E	LDL precursor	38	30	8	23	11
Low-density lipoprotein	1.019–1.063	18–25	B-100	Cholesterol transport	10	38	8	22	21
High-density lipoprotein	1.063–1.21	7.5–20	A	Reverse cholesterol transport	5–10	14–21	3–7	19–29	33–57

80. b) VLDL

Very low density lipoproteins (VLDL): They are produced in liver and intestine and are responsible for the transport of endogenously synthesized triacylglycerols.

Small quantities of VLDL are also to be found in chyle; however, most VLDL in the plasma are of hepatic origin. They are the vehicles of transport of triacylglycerol from the liver to the extrahepatic tissues.

81. c) HDL

[Ref: Harper's Illustrated biochemistry, 30th Edition]

				Composition			
Lipoprotein	Source	Diameter (nm)	Density (g/mL)	Protein (%)	Lipid (%)	Main Lipid Components	Apollpoproteins
Chylomicrons	Intestine	90-1000	<0.95	1-2	98-99	Triacylglycerol	A-I, A-II, A-IV, B-48, C-I, C-II, C-III, E
Chylomicrons remnants	Chylomicron	45-150	<1.006	6-8	92-94	Triacylglycerol, phospholipids, cholesterol	8-48, E
VLDL	Liver (Intestine)	30-90	0.95-1.006	7-10	90-93	Triacylglycerol	B-100, C-I, C-II, C-III
IDL	VLDL	25-35	1.006-1.019	11	89	Triacylglycerol, cholesterol	B-100, E
LDL	VLDL	20-25	1.019-1.063	21	79	Cholesterol	B-100
HDL	Liver, Intestine, VLDL, chylomicrons					Phospholipids, cholesterol	A-I, AII, A-IV, C-I, C-II, C-III, D," E
HDL_1		20-25	1.019-1.063	32	68		
HDL_2		10-20	1.063-1.125	33	67		
HDL_3		5-10	1.125-1.210	57	43		
Preβ-HDL[c]		<5	>1.210				A-I
Albumin / free fatty acids	Adipose tissue		> 1.281	99	1	Free fatty acids	

aSecreted with chylomicrons but transfers to HDL.

bAssociated with HDL2 and HDL3 subfractions.

cPart of a minor fraction known as very high density lipoproteins (VHDL).

Abbreviations: HDL, high-density lipoproteins; IDL, intermediate-density lipoproteins; LDL, low-density lipoproteins; VLDL, very low density lipoproteins.

82. d) HDL

[Ref: Stryer 8th Edition]

Although the events that result in atherosclerosis take place rapidly in familial hypercholesterolemia, a similar sequence of events take place in people who develop atherosclerosis over decades. In particular, the formation of foam cells and plaques are especially hazardous occurrences. HDL and its role in returning cholesterol to the liver appear to be important in mitigating these life-threatening circumstances. HDL has a number of antiatherogenic properties, including the inhibition of LDL oxidation, but the best-characterized

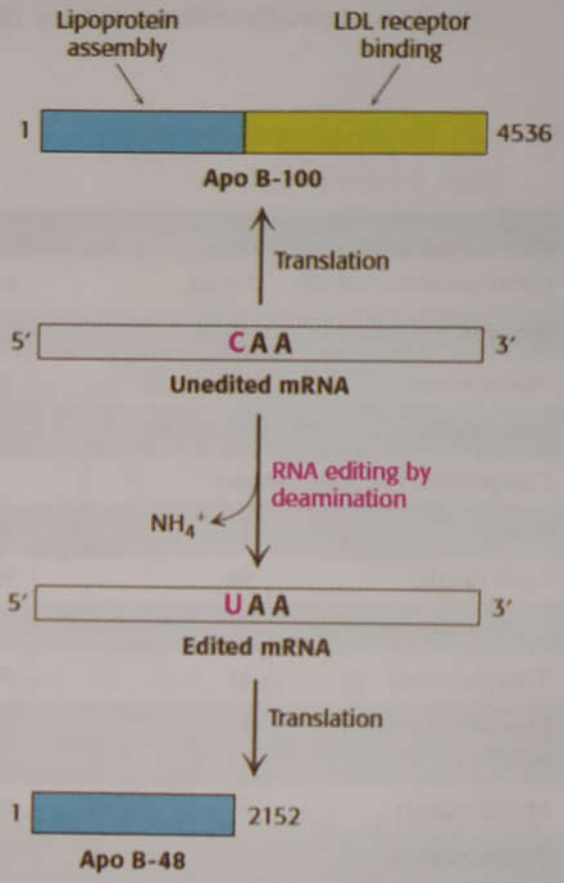
property is the removal of cholesterol from cells, especially macrophages. Earlier, we learned that HDL retrieves cholesterol from other tissues in the body to return the cholesterol to the liver for excretion as bile or in the feces. This transport, called reverse cholesterol transport, is especially important in regard to macrophages. Indeed, when the transport fails, macrophages become foam cells and facilitate the formation of plaques. Macrophages that collect cholesterol from LDL normally transport the cholesterol to HDL particles. The more HDL, the more readily this transport takes place and the less likely that the macrophages will develop into foam cells. Presumably, this robust reverse cholesterol transport accounts for the observation that higher HDL levels confer protection against arthrosclerosis. Indeed, efforts are underway to develop drugs that will boost the levels of HDL in the blood. The importance of reverse cholesterol transport is illustrated by the occurrence of mutations that inactivate one of the cholesterol-transport proteins in macrophages. This transport is facilitated by members of the ABC class of transport proteins present in macrophage membranes. Loss of activity of cholesterol-transport protein ABAC1 results in a very rare condition called Tangier disease, which is characterized by HDL deficiency, accumulation of cholesterol in macrophages, and premature atherosclerosis.

Another antiatherogenic property of HDL is due to the association of a serum esterase, paraoxanase, with HDL. Paraoxanase may destroy oxLDL, accounting for some of HDL's ability to protect against coronary disease.

83. b) RNA editing

[Ref: Stryer 8th Edition]

Apo B-100, one of the largest proteins known (513 kd), is a longer version of apo B-48. Both apo B proteins are encoded by the same gene and produced from the same initial RNA transcript. In the intestine, RNA editing modifies the transcript to generate the mRNA for apo B-48, the truncated form.



RNA editing. Enzyme catalyzed deamination of a specific cytidine residue in the mRNA for apolipoprotein B-100 changes a codon for glutamine (CAA) to a stop codon (UAA). Apolipoprotein B-48, a truncated version of the protein lacking the LDL receptor-binding domain, is generated by this posttranscriptional change in the mRNA sequence.

84. c) Decreased production of LDL receptor in the adipose tissue and increased release of cholesterol from adipose tissues

Primary Disorders of the Plasma Lipoproteins (Dyslipoproteinemias) Are Inherited Inherited defects in lipoprotein metabolism lead to the primary condition of either hypo- or hyperlipoproteinemia . For

example, familial hypercholesterolemia (FH), causes severe hypercholesterolemia and is also associated with premature atherosclerosis. The defect is most often in the gene for the LDL receptor, so that LDL is not cleared from the blood. In addition, diseases such as diabetes mellitus, hypothyroidism, kidney disease (nephrotic syndrome), and atherosclerosis are associated with secondary abnormal lipoprotein patterns that are very similar to one or another of the primary inherited conditions. Virtually all of the primary conditions are due to a defect at a stage in lipoprotein formation, transport, or degradation. Not all of the abnormalities are harmful.

85. a) Chylomicrons

[Ref: Stryer 8th Edition]

Characteristic	Chylomicrons	VLDL	LDL	HDL
Electrophoretic mobility	Origin	Pre-β	β	α
Density	<0.96	0.96-1.006	1.006-1.063	1.063-1.21
Diameter (nm)	100- 1,000	30-90	20-25	10-20
Apoproteins	AI, AII B_{48}	B_{100}. CI. CII CIII, E	B_{100}	AI, AII, CI, CII, CIII, D, E
Composition (%, approximate)				
Protein	2	10	20	40
Lipid (total)	98	90	80	60
Lipid components (%)				
Triacylglycerol	88	55	12	12
Cholesterol (free and ester)	4	24	59	40
Phospholipids	8	20	28	47
Free tatty acids	-	1	1	1

86. d) Does not require CII as cofactor

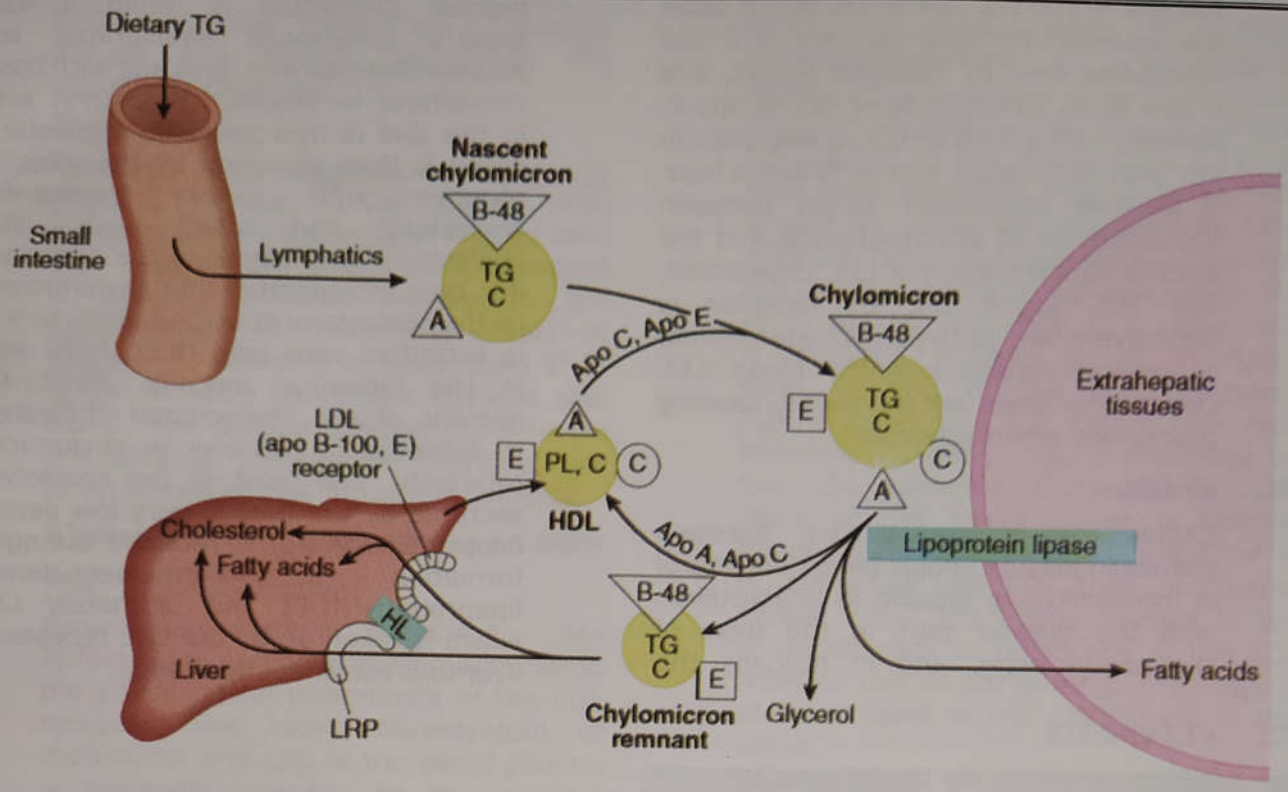
Lipoprotein lipase is located on the walls of blood capillaries, anchored to the endothelium by negatively charged proteoglycan chains of heparan sulfate. It has been found in heart, adipose tissue, spleen, lung, renal medulla, aorta, diaphragm, and lactating mammary gland, although it is not active in adult liver. It is not normally found in blood; however, following injection of heparin, lipoprotein lipase is released from its heparan sulfate binding sites into the circulation.

Both phospholipids and apo C-II are required as cofactors for lipoprotein lipase activity, while apo A-II and apo C-III act as inhibitors.

87. a) Chylomicrons

By definition, chylomicrons are found in chyle formed only by the lymphatic system draining the intestine. They are responsible for the transport of all dietary lipids into the circulation.

88.



Metabolic fate of chylomicrons. (A, apolipoprotein A; B-48, apolipoprotein B-48; C, apolipoprotein C; C, cholesterol and cholesteryl ester; E, apolipoprotein E; HDL, high-density lipoprotein; HL, hepatic lipase; LRP, LDL-receptor-related protein; PL, phospholipid; TG, triacylglycerol.) Only the predominant lipids are shown.

88. d) Apo B

The Distribution of Apolipoproteins Characterizes the Lipoprotein One or more apolipoproteins (proteins or polypeptides) are present in each lipoprotein. They are usually abbreviated as apo followed by the letter A, B, C, etc .Some apolipoproteins are integral and cannot be removed (eg, apo B), whereas others are bound to the surface and are free to transfer to other lipoproteins, eg, apos C and E). The major apolipoproteins of HDL (α-lipoprotein) are apoAs. The main apolipoprotein of LDL (β-lipoprotein) is apo B (B-100), which is found also in VLDL. Chylomicrons contain a truncated form of apo B (B-48) that is synthesized in the intestine, while B-100 is synthesized in the liver.

Apos C-I, C-II, and C-III are smaller polypeptides (molecular mass 70009000 Da) freely transferable between several different lipoproteins.

Apo E, found in VLDL, HDL, chylomicrons, and chylomicron remnants, is also freely transferable; it accounts for 5% to 10% of total VLDL apolipoproteins in normal subjects.

89. b) HDL

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Plasma LCAT Is Responsible for Virtually All Plasma Cholesteryl Ester in Humans Lecithin: cholesterol acyltransferase (LCAT) activity is associated with HDL containing apo A-I. As cholesterol in HDL becomes esterified, it creates a concentration gradient and draws in cholesterol from tissues and from other lipoproteins , thus enabling HDL to function in reverse cholesterol transport .

90. c) Apo E and Apo B 100

Ldl is metabolized via the ldl receptor

The liver and many extrahepatic tissues express the LDL (apo B-100, E) receptor. It is so designated because it is specific

for apo B-100 but not B-48, which lacks the carboxyl terminal domain of B-100 containing the LDL receptor ligand, and it also takes up lipoproteins rich in apo E. Approximately 30% of LDL is degraded in extrahepatic tissues and 70% in the liver. A positive correlation exists between the incidence of atherosclerosis and the plasma concentration of LDL cholesterol. The LDL (apoB-100, E) receptor is defective in familial hypercholesterolemia, a genetic condition which blood LDL cholesterol levels are increased, causing premature atherosclerosis .

91. a) LDL

Cholesterol is transported between tissues in plasma lipoproteins Cholesterol is transported in plasma in lipoproteins, with the greater part in the form of cholesteryl ester, and in humans the highest proportion is found in LDL. Dietary cholesterol equilibrates with plasma cholesterol in days and with tissue cholesterol in weeks. Cholesteryl ester in the diet is hydrolyzed to cholesterol, which is then absorbed by the intestine together with dietary unesterified cholesterol and other lipids. With cholesterol synthesized in the intestines, it is then incorporated into chylomicrons. Of the cholesterol absorbed, 80% to 90% is esterified with long-chain fatty acids in the intestinal mucosa. Ninety-five percent of the chylomicron cholesterol is delivered to the liver in chylomicron remnants, and most of the cholesterol secreted by the liver in very low density lipoprotein (VLDL) is retained duringthe formation of intermediate-density lipoprotein (IDL) and ultimately LDL, which is taken up by the LDL receptor in liver and extrahepatic tissues.

92. c) Type III

Ldl is metabolized via the ldl receptor

Name	Defect	Remarks
Hyperlipoproteinemias Familial lipoprotein lipase deficiency (type 1)	Hypertriacylglycerolemia due to deficiency of LPL, abnormal LPL, or apo C-ll deficiency causing inactive LPL.	Slow clearance of chylomicrons and VLDL. Low levels of LDL and HDL. No increased risk of coronary disease.
Familial hypercholesterolemia (type Ma)	Defective LDL receptors or mutation in ligand region of apo B-100.	Elevated LDL levels and hypercholesterolemia, resulting in atherosclerosis and coronary disease.
Familial type III hyperlipoproteinemia (broad beta disease, remnant removal disease, familial dysbetalipoproteinemia	Deficiency in remnant clearance by the liver is due to abnormality in apo E. Patients lack isoforms E3 and E4 and have only E2, which does not react with the E receptor.*	Increase in chylomicron and VLDL remnants of density <1.019 ((J-VLDL). Causes hypercholesterolemia, xanthomas, and atherosclerosis.
Familial hypertriacylglycerolemia (type IV)	Overproduction of VLDL often associated with glucose intolerance and hyperinsulinemia.	Cholesterol levels rise with the VLDL concentration. LDL and HDL tend to be subnormal. This type of pattern is commonly associated with coronary heart disease, type II diabetes mellitus, obesity, alcoholism, and administration of progestational hormones.

93. c) HDL

In abetalipoproteinemia (a rare disease), lipoproteins containing apo B are not formed and lipid droplets accumulate in the intestine and liver.

Abetalipoproteinemia: This is a rare disorder due to a defect in the synthesis of apoprotein B. It is characterized by a total absence of B-lipoprotein (LDL) in plasma. Triacylglycerols are not found in plasma, but they accumulate in liver and intestine. Serum cholesterol level is low. Abetalipoproteinemia is associated with decreased absorotion of fat and fat-

soluble vitamins, Impairment in physical growth and mental retardation are commonly observed.

Add a note on:

Familial alpha-lipoprotein deficiency (Tangier disease) : The plasma HDL particles are almost absent. Due to this, the reverse transport of cholesterol is severely affected leading to the accumulation of cholesteryl esters in tissues. An absence of apoprotein C II-which activates lipoprotein lipase-is also found. The plasma triacylglycerol levels are elevated. The affected individuals are at an increased risk for atherosclerosis.

94. b) Absence of LDL receptors on cells

[Ref: Stryer 8th Edition]

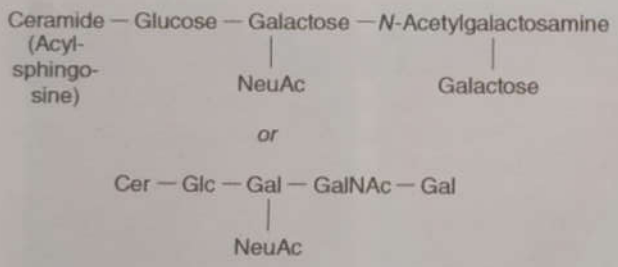
Brown and Goldstein's pioneering studies of familial hypercholesterolemia revealed the physiological importance of the LDL receptor. The total concentration of cholesterol and LDL in the blood plasma is markedly elevated in this genetic disorder, which results from a mutation at a single autosomal locus. The cholesterol level in the plasma of homozygotes is typically 680 mg dl−1, compared with 300 mg dl−1 in heterozygotes (clinical assay results are often expressed in milligrams per deciliter, which is equal to milligrams per 100 milliliters). A value of < 200 mg dl−1 is regarded as desirable, but many people have higher levels. In familial hypercholesterolemia, cholesterol is deposited in various tissues because of the high concentration of LDL cholesterol in the plasma. Nodules of cholesterol called xanthomas are prominent in skin and tendons. Of particular concern is the oxidation of the excess blood LDL to form oxidized LDL (oxLDL). The oxLDL is taken up by immune-system cells called macrophages, which become engorged to form foam cells. These foam cells become trapped in the walls of the blood vessels and contribute to the formation of atherosclerotic plaques that cause arterial narrowing and lead to heart attacks . In fact, most homozygotes die of coronary artery disease in childhood. The disease in heterozygotes (1 in 500 people) has a milder and more variable clinical course. The molecular defect in most cases of familial hypercholesterolemia is an absence or deficiency of functional receptors for LDL. Receptor mutations that disrupt each of the stages in the endocytotic pathway have been identified. Homozygotes have almost no functional receptors for LDL, whereas heterozygotes have about half the normal number. Consequently, the entry of LDL into liver and other cells is impaired, leading to an increased level of LDL in the blood plasma. Furthermore, less IDL enters liver cells because IDL entry, too, is mediated by the LDL receptor. Consequently, IDL stays in the blood longer in familial hypercholesterolemia, and more of it is converted into LDL than in normal people. All deleterious consequences of an absence or deficiency of the LDL receptor can be attributed to the ensuing elevated level of LDL cholesterol in the blood.

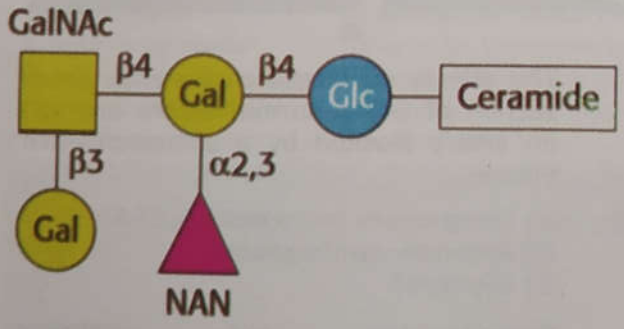
The effects of excess cholesterol. Cross section of (A) a normal artery and (B) an artery blocked by a cholesterol-rich plaque.

95. a) Long chain fatty acid (LCFA)
b) Alcohol- sphingosine
d) Glycerol

Gangliosides are complex glycosphingolipids derived from glucosylceramide that contain in addition one or more molecules of a sialic acid. Neuraminic acid (NeuAc) is the principal sialic acid found in human tissues. Gangliosides are also present in nervous tissues in high concentration. They function in cell-cell recognition and communication and as receptors for hormones and

bacterial toxins such as cholera toxin. The simplest ganglioside found in tissues is GM3, which contains ceramide(The combination of sphingosine plus fatty acid is known as ceramide, a structure also found in the glycosphingolipids), one molecule of glucose, one molecule of galactose, and one molecule of NeuAc. In the shorthand nomenclature used, G represents ganglioside; M is a monosialo-containing species; and the subscript 3 is a number assigned on the basis of chromatographic migration. GM1 a more complex ganglioside derived from GM3, is of considerable biologic interest, as it is known to be the receptor in human intestine for cholera toxin. Other gangliosides can contain anywhere from one to five molecules of sialic acid, giving rise to di-, trisialogangliosides, etc.

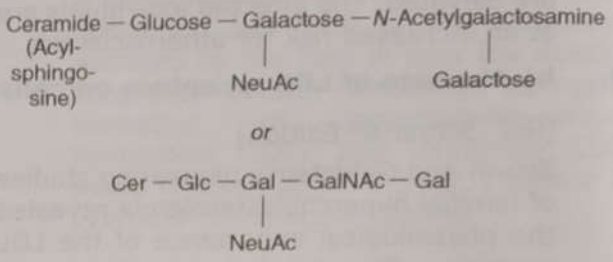




Ganglioside GM1. This ganglioside consists of five monosaccharides linked to ceramide: one glucose (Glc) molecule, two galactose (Gal) molecules, one N-acetylgalactosamine(GalNAc) molecule, and one N- acetylneuraminate (NAN) molecule.

96. a) N-Acetyineuraminic acid (NANA), hexoses sphingosine, long chain fatty acid

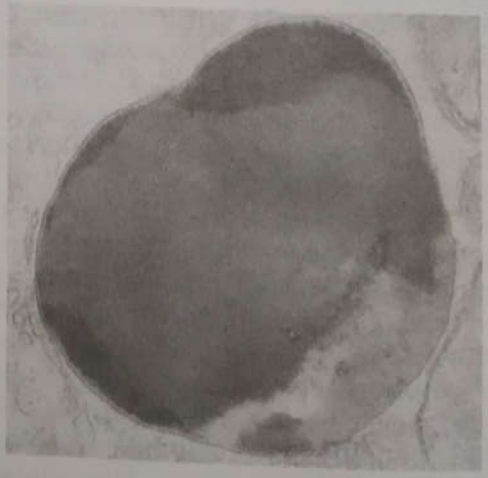
Gangliosides are complex glycosphingolipids derived from glucosylceramide that contain in addition one or more molecules of a sialic acid. Neuraminic acid (NeuAc) is the principal sialic acid found in human tissues. Gangliosides are also present in nervous tissues in high concentration. They function in cell-cell recognition and communication and as receptors for hormones and bacterial toxins such as cholera toxin.



97. b) Hexosaminidase A

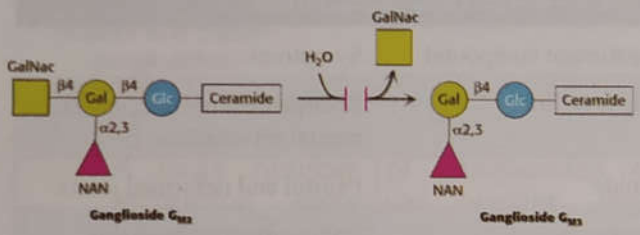
[Ref: Stryer 8th Edition]

Tay–Sachs disease is caused by a failure of lipid degradation: an inability to degrade gangliosides. Gangliosides are found in highest concentration in the nervous system, particularly in gray matter, where they constitute 6% of the lipids. Gangliosides are normally degraded inside lysosomes by the sequential removal of their terminal sugars but, in Tay–Sachs disease, this degradation does not take place. As a consequence, neurons become significantly swollen with lipid-filled lysosomes .



Lysosome with lipids. An electron micrograph of a lysosome containing an abnormal amount of lipid.

An affected infant displays weakness and retarded psychomotor skills before 1 year of age. The child is demented and blind by age 2 and usually dies before age The ganglioside content of the brain of an infant with Tay–Sachs disease is greatly elevated. The concentration of ganglioside GM2 is many times higher than normal because its terminal N-acetylgalactosamine residue is removed very slowly or not at all. The missing or deficient enzyme is a specific -Nacetylhexosaminidase.



Tay–Sachs disease can be diagnosed in the course of fetal development. Amniotic fluid is obtained by amniocentesis and assayed for b-Nacetylhexosaminidase activity.

98. c) Lysosome

Sphingolipidoses:

Lipid storage diseases, representing IysosomaI storage defects, are inherited disorders. They are characterized by the accumulation of complex lipids.

The term sphingolipidoses is often used to collectively refer to the genetic disorders that lead to the accumulation of any one of the sphingolipids (Glycosphingolipids and sphingomyelins).

99. b) Niemann-Pick disease

[Ref: Harper's Illustrated biochemistry, 30th Edition]

The sphingolipidoses (lipid storage diseases) are a group of inherited diseases that are caused by a genetic defect in the catabolism of lipids containing sphingosine. They are part of a larger group of lysosomal disorders and exhibit several constant features: (1) complex lipids containing ceramide accumulate in cells, particularly neurons, causing neurodegeneration and shortening the lifespan. (2) The rate of synthesis of the stored lipid is normal. (3) The enzymatic defect is in the lysosomal degradation pathway of sphingolipids. (4) The extent to which the activity of the affected enzyme is decreased is similar in all tissues. There is no effective treatment for many of the diseases, although some success has been achieved with enzyme replacement therapy and bone marrow transplantation in the treatment of Gaucher and Fabry diseases. Other promising approaches are substrate deprivation therapy to inhibit the synthesis of sphingolipids and chemical chaperone therapy. Gene therapy for lysosomal disorders is also currently under investigation. Some examples of the more important lipid storage diseases are shown in

Disease	Enzyme Deficiency	Lipid Accumulating	Clinical Symptoms
Tay-Sachs disease	Hexosaminidase A	Cer—Glc—Gal(NeuAc)-GalNAc G_{m2} Ganglioside	Mental retardation, blindness, muscular weakness
Fabry disease	α-Galactosidase	Cer—Glc—Gal—Gal Globotriaosylceramide	Skin rash, kidney failure (full symptoms only in males; X-linked recessive)
Metachromatic leukodystrophy	Arylsulfatase A	Cer—Gal—$0S0_3$ 3-Sulfogalactosylceramlde	Mental retardation and psychologic disturbances In adults; demyelination
Krabbe disease	β-Galactosidase	Cer—Gal Galactosylceramide	Mental retardation; myelin almost absent

Gaucher disease	β-Glucosidase	Cer—Glc Glucosylceramide	Enlarged liver and spleen, erosion of long bones, mental retardation in Infants
Nlemann-Pick disease	Sphingomyelinase	Cer—P—choline Sphingomyelin	Enlarged liver and spleen, mental retardation; fatal in early life
Farber disease	Ceramldase	Acyl—Sphingoslne Ceramlde	Hoarseness, dermatitis, skeletal deformation, mental retardation; fatal In early life

Multiple sulfatase deficiency results in accumulation of sulfogalactosylceramide, steroid sulfates, and proteoglycans owing to a combined deficiency of arylsulfatases A, B, and C and steroid sulfatase.

100. c) Sphingomyelinase

[Ref: Satyanarayan 4th Edition]

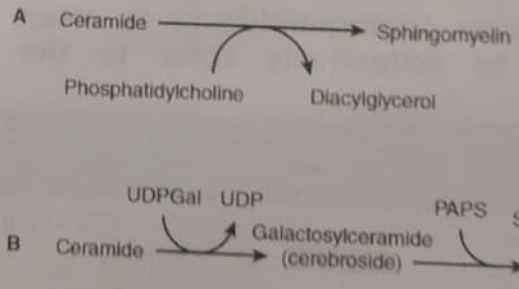
TAB if 14.4 Some examples of sphingolipldoses (lipid storage diseases) with their characteristics 1

Disease	Missing/defective enzyme	Major storage compound	Symptoms
Niemann-Pick disease	Sphingomyelinase	Sphingomyelins	Enlargement of liver, spleen, mental retardation.
Farter's disease	Ceramidase	Ceramide	Painful and deformed joints.
Gaucher's disease	β-Giucosidase	Glucoceretoroside	Enlargement of liver and spleen, osteoporosis, mental retardation.
Krabbe's disease	β-Galactosidase	Galactocerebrosides	Absence of myelin formation, liver and spleen enlargement, mental retardation.
Tay-Sachs disease	Hexosaminidase A	Ganglioside GM_2	Blindness, mental retardation, death within 2-3 years.
Fabry's disease	α-Galactosidase	Ceramide trihexoside	Renal failure, skin rash, pain in lower extremities.

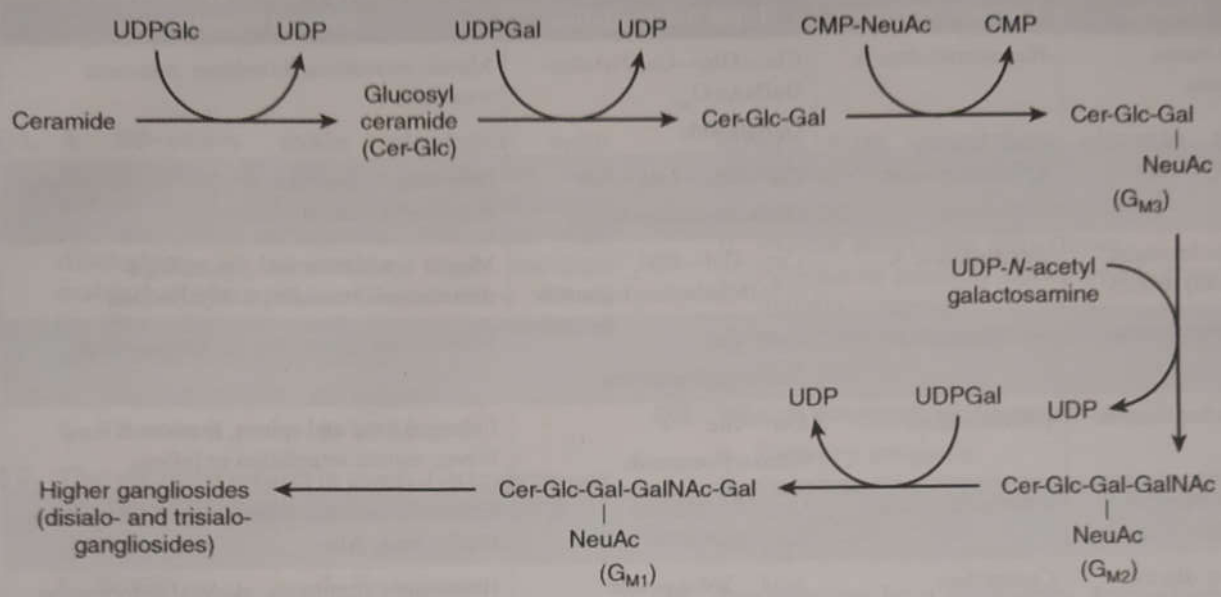
101. d) Sphinogosine

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Glycosphingolipids Are a Combination of Ceramide With One or More Sugar Residues The simplest glycosphingolipids (cerebrosides) are galactosylceramide (GalCer) and glucosylceramide (GlcCer). GalCer is a major lipid of myelin, whereas GlcCer is the major glycosphingolipid of extraneural tissues and a precursor of most of the more complex glycosphingolipids. GalCer is formed in a reaction between ceramide and UDPGal (formed by epimerization from UDPGlc).



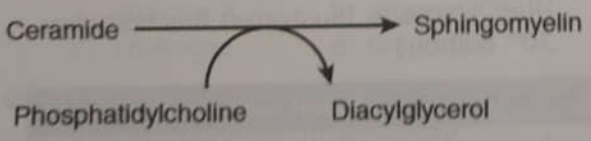
Sulfogalactosylceramide and other sulfolipids such as the sulfo(galacto)-glycerolipids and the steroid sulfates are formed after further reactions involving 3′-phosphoadenosine5′-phosphosulfate (PAPS; "active sulfate"). Gangliosides are synthesized from ceramide by the stepwise addition of activated sugars (eg, UDPGlc and UDPGal) and a sialic acid, usually N-acetylneuraminic acid.



A large number of gangliosides of increasing molecular weight may be formed. Most of the enzymes transferring sugars from nucleotide sugars (glycosyl transferases) are found in the Golgi apparatus. Glycosphingolipids are constituents of the outer leaflet of plasma membranes and are important in cell adhesion and cell recognition. Some are antigens, for example, ABO blood group substances. Certain gangliosides function as receptors for bacterial toxins (eg, for cholera toxin, which subsequently activates adenylyl cyclase).

102. b) Sphingomyelin

[Ref: Harper's Illustrated biochemistry, 30th Edition]



Sphingomyelins are phospholipids and are formed when ceramide reacts with phosphatidylcholine to form sphingomyelin plus diacylglycerol.This occurs mainly in the Golgi apparatus and to a lesser extent in the plasma membrane.

103. b) Beta-Glucosidase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

The sphingolipidoses (lipid storage diseases) are a group of inherited diseases that are caused by a genetic defect in the catabolism of lipids containing sphingosine. They are part of a larger group of lysosomal disorders and exhibit several constant features: (1) complex lipids containing ceramide accumulate in cells, particularly neurons, causing neurodegeneration and shortening the lifespan. (2) The rate of synthesis of the stored lipid is normal. (3) The enzymatic defect is in the lysosomal degradation pathway of sphingolipids. (4) The extent to which the activity of the affected enzyme is decreased is similar in all tissues. There is no effective treatment for many of the diseases, although some success has been achieved with enzyme replacement therapy and bone marrow transplantation in the treatment of Gaucher and Fabry diseases. Other promising approaches are substrate deprivation therapy to inhibit the synthesis of sphingolipids and chemical chaperone therapy. Gene therapy for lysosomal disorders is also currently under investigation. Some examples of the more important lipid storage diseases are shown in

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Niemann-Pick disease	Sphingomyelinase	Cer—P—choline Sphingomyelin	Enlarged liver and spleen, mental retardation; fatal in early life
Farber disease	Ceramidase	Acyl—Sphingosine Ceramide	Hoarseness, dermatitis, skeletal deformation, mental retardation; fatal In early life

A dozen or so glycolipid storage diseases have been described (eg, Gaucher's disease and TaySachs disease), each due to a genetic defect in the pathway for glycolipid degradation in the lysosomes. Most common lysosomal storage disorder .

Intravenous infusion of recombinantly produced glycosylases has been approved for the treatment of several lysosomal storage diseases including the Gaucher disease (β-glucosidase), Pompe disease (α-glucosidase), Fabry disease (α-galactosidase A), and Sly disease (β-glucuronidase).

104. c) Iduronate Sulfatase

Ref: Harper's Illustrated biochemistry, 30th Edition]

The mucopolysaccharidoses (MPSs) share a common mechanism of causation, as illustrated:

Simplified scheme of causation of a mucopolysaccharidosis, such as the Hurler syndrome.

Mutation(s) in a gene encoding a lysosomal hydrolase involved in the degradation of one or more GAGs

↓

Defective lysosomal hydrolase

↓

Accumulation of substrate in various tissues, including live, spleen, bone, skin and central nervous system

105. d) Arylsulfatase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Disease	Enzyme Deficiency	Lipid Accumlating	Clinical Symptoms
Metachromatic leukodystrophy	Arylsulfatase A	Cer - Gal - OSO_3 3- Sulfogalactosylceramide	Mental retardation and psychologic disturbances in adults; demyelination

Vitamins and Minerals – Questions

Q1. A 50-years male alcoholic with symptoms of fatigue and he has swelling of feet and loss of sensations in legs and anaemia. He also has dilatation of ventricle, high cardiac output state and cardiac failure. What is the vitamin deficiency associated with this presentation?

a. Vitamin B_1
b. Vitamin B_2
c. Vitamin B_{12}
d. Vitamin B_3

Q2. The vitamin which is useful in treatment of type IIb hyperlipoproteinemia is

a. Thiamine
b. Riboflavin
c. Niacin
d. Pyridoxine

Q3. Vitamin K in its coenzyme form is regenerated by which enzyme?

a. Glutathione reductase
b. Pyruvate Carboxylase
c. Dihydrofolate reductase
d. Epoxide reductase

Q4. A middle aged woman presents with fissures in mouth, tingling sensation and peripheral neuropathy. Investigations showed reduced glutathione reductase activity. Which vitamin deficiency is the likely cause of this?

a. Vitamin B1
b. Vitamin B2
c. Vitamin B6
d. Vitamin B 12

Q5. Fe absorption increases by which vitamin?

a. Vitamin A
b. Vitamin C
c. Thiamine
d. Riboflavin

Q6. Role of vitamin K in epoxide cycle is

a. Carboxylation of aspartate
b. Dehydrogenation of glutamate
c. Carboxylation of glutamate
d. Dehydrogenation of aspartate

Q7. Which of the following statement (s) is/are true regarding vitamin B12 deficiency:

a. ↓Erythocyte transketolase level
b. Muscle weakness may occur
c. Peripheral sensory nerve involvement is usually present
d. Neuronal symptom improves with Vit. B12 therapy

Q8. Which enzyme utilizes zinc?

a. Salivary amylase
b. Catalase
c. Pancreatic lipase
d. Alkaline phosphatase

Q9. Pyridoxine is a co-factor for which of the following reaction?

a. Dehydrogenation
b. Carboxylation
c. Decarboxylation
d. Acetylation

Q10. The vitamin requirement that increases with increased protein intake:

a. Niacin
b. Pyridoxine
c. Thiamine
d. Tocopherol

Q11. What is function of intrinsic factor:

a. Increases cobalamin absorption pattern
b. Increase folate absorption
c. Coverts prothrombin to thrombin
d. converts fibrinogen to fibrin

Q12. Diagnosis of folic acid deficiency is done by:

a. FIGLU estimation
b. Peripheral blood smears
c. AICAR estimation
d. All the above

Q13. Which amino acid does not take part in one carbon transfer reactions?

a. Glycine
b. Serine
c. Alanine
d. Histidine

1. a	2. c	3. d	4. b	5. b	6. c	7. b, c, d	8. d	9. c	10. b
11. a	12. d	13. c							

Q14. The mineral having action like vitamin E

a. calcium
b. Iron
c. Selenium
d. Magnesium

Q15. Ceruloplasmin contains

a. Zn
b. Cu
c. Se
d. Fe

Q16. In Wilsons disease copper accumulate in all EXCEPT

a. Liver
b. Eye
c. Brain
d. Spleen

Q17. The cofactor required for the activity of the enzyme xanthine oxidase is

a. Copper
b. Molybdenum
c. Zinc
d. Selenium

Q18. Which of the following trace elements is important for conversion of procollagen to collagen ?

a. Se
b. Cu
c. Zn
d. Mg

Q19. Cytochrome Oxidase contains

a. Copper
b. Iodine
c. Magnanes
d. Molybdenum

Q20. Lyslyl oxidase requires

a. Zn
b. Cu
c. Fe
d. Mg

Q21. Pyruvate utilization in tissue is decreased in:

a. Pernicious anemia
b. Scurvy
c. Beriberi
d. Pellagra

Q22. Diagnosis of vitamin B1 deficiency is made by

a. Thiamine level
b. Transketolase activity
c. Carboxylase activity
d. Transaminase activity

Q23. Which Vitamin deficiency cause glossitis and cheilosis?

a. Thiamin
b. Riboflavin
c. Folic acid
d. Vitamin A

Q24. Only vitamin that help in carbon fixation

a. Folic acid
b. Pantothenic acid
c. Niacin
d. Thiamine

Q25. Which of the following requires Vitamin B_{12}?

a. Serilie to lysine
b. Homocysteine to methionine
c. Serine to glycine
d. Glutarmine to glutamate

Q26. Transamination reaction requires

a. Biotin
b. Folic acid
c. Pyrdoxine
d. Niacin

Q27. Vitamin B_6 deficiency cause increased excretion of

a. Methylmalonyl CoA
b. Xanthurenic acid
c. Branched chain ketoacids
d. Ketone Bodies

Q28. CoA requires

a. Pantothenic group
b. Biotin
c. Folic acid
d. Cabalamine

Q29. Vitamin required for collagen synthesis

a. Vitamin A
b. Vitamin C
c. Thiamine
d. Folic acid

Q30. Decarboxylation reaction require

a. Riboflavin
b. Thiamine
c. Niacin
d. Biotin

Q31. Which of the following is rate limiting step?

a. 25 hydroxylation of vitamin D
b. 24 hydroxylation of vitamin D
c. 1 hydroxylation of vitamin D
d. None

Q32. Niacin deficiency is seen among people consuming ..... based diets

a. Rice
b. Pulses
c. Millets
d. EGG

14. c	15. b	16. d	17. b	18. b	19. a	20. b	21. c	22. b	23. b
24. a	25. b	26. c	27. b	28. a	29. c	30. b	31. c	32. c	

Q33. Vitamin B12 deficiency is not associated with
a. Megaloblastic abenia'
b. Subacute combined degeneration of spinal cord
c. Microcytic anemia

Q34. Vitamin synthesized by Intestinal bacteria are
a. A and K
b. C and K
c. A and E
d. K and B

Q35. Vitamin K epoxide cycle is seen in
a. Liver
b. Lungs
c. Spleen
d. Intestine

Q36. Riboflavin deficiency is assessed by
a. Transketolase
b. Glutathione reductase
c. PDH
d. None

Q37. Major form of folic acid to transfer one carbon is
a. Methylene THF
b. Formyl THF
c. Methyl THF
d. All

Q38. Which Vitamin is involved in Redox reactions?
a. Pyridoxine
b. Biotin
c. Folic acid
d. Riboflavin

Q39. Major function of Vitamin E in the body
a. Regulation of energy metabolism
b. Carboxylation reaction
c. Blood clotting
d. Protection of Biological membrane from free radical damage

Q40. Neurotoxicity is seen with excess of
a. Vitamin B6
b. Vitamin B12
c. Vitamin B2
d. Vitamin C

Q41. Not obtained from plant source
a. Cobalamine
b. Riboflavin
c. Thiamine
d. Vitamin A

Q42. Conversion of glycine to Serine requires
a. Folic acid
b. Thiamine
c. Vitamin C
d. Fe2+
e. Pyridoxal phosphate

Q43. The vitamin which is useful in treatment of type IIb hyperlipoproteinemia is
a. Thiamine
b. Riboflavin
c. Niacin
d. Pyridoxine

Q44. Which is not Pyridoxine dependent?
a. Oxaluria
b. Homocystinurea
c. Maple syrup urine Disease
d. Xanthenuric aciduria

Q45. All are vitamin K dependent clothing factors of Hepatic origin except
a. II
b. VII
c. VIII
d. X

Q46. Thiamine deficiency is known to occur in all of the following except
a. Food faddist
b. Homocystinemia
c. Chronic alcoholic
d. Chronic heart failure

Q47. The activity of the following enzyme is affected by biotin deficiency
a. Transketolase
b. Dehydrogenase
c. Oxidase
d. Carboxylase

Q48. Which coenzyme is responsible for carboxylation reaction?
a. Biotin
b. FAD
c. NADH
d. Thiamine pyrophosphate

Q49. Nicotinamide is derived from
a. Histidine
b. Methionine
c. Tryptophan
d. Phenylalanine

Q50. Tryptophan is used in synthesis of which vitamin?
a. B1
b. B2
c. B3
d. B12

Q51. Pyridoxine deficiency affect.... metabolism:
a. Phenylalanine
b. Tryptophan
c. Leucine
d. Lysine

33. c	34. d	35. a	36. b	37. a	38. d	39. d	40. a	41. a	42. a
43. c	44. c	45. c	46. b	47. d	48. d	49. c	50. c	51.	

Q52. Vitamin B_{12} is

a. Extrinsic factor of castle
b. Intrinsic factor of castle
c. Cyanocbalamine
d. Decrease ca2 + decrease po4

Q53. Vitamin C is present is largest amount n the body in

a. Eye
b. kidney
c. Testes
d. Adrenal cortex

Q54. Treatment to multiple carboxylase deficiency is

a. Biotin
b. Pyridoxine
c. Thiamine
d. Folic acid

Q55. Which of the following statement about thiamine is true ?

a. It is a coenzyme of lactate dehydrogenase
b. It deficiency is associated with scurvy
c. its coenzyme function is done by thiamine monophosphate
d. It is coenzyme for pyruvate dehydrogenase and alpha ketoglutarte dehydrogense

Q56. Carboxylation of clotting factors by vitamin K is required to be biologically active. Which of the following amino acid is carboxylated

a. Histidine
b. Histamine
c. Glutamate
d. Aspartate

Q57. A vitamin related to a cofactor in glycine metabolism is:

a. Vitamin E
b. Folic acid
c. Thiamine
d. Cobalamine
e. pantothenic acid

Q58. Two vitamins whose derivatives are involved in transformation of serine to glycine are :

a. B_6 and B_2
b. B_{12} and nicotinamide
c. Folic acid and B_6
d. Folic acid

Q59. Vitamin E prevents rancidity by virtue of its property

a. Antioxidant
b. Oxidant
c. Sulfuration
d. Hydrogenation

Q60. A low serum carotene level is caused by

a. Vit A deficiency
b. Intrinsic factor deficiency
c. malabsorption syndrome
d. Achlorhydria

Q61. Following Vitamin prevents peroxidation of lipids of cellular level

a. Vitamin A
b. Vitamin C
c. Vitamin E
d. Vitamin K

Q62. Which of the following is a component of the visual pigment rhodopsin?

a. beta – carotene
b. Retinal
c. Retinol
d. Retinoic acid

Q63. Amino acid involved in 1 carbon metabolism

a. Folic acid
b. Thiamine
c. Pyridoxine
d. None

Q64. Principal function of cyanocobalamin is

a. Post translation carboxlation of protein
b. Acts as coenzymes for methionine synthase and L methyl melonyl CoA synthase
c. A coenzyme for one carbone transfer in nucleic acid mertbolism
d. A cofactor for decarboxylase of ketoacid

Q65. Thiamine pyroposphate in coenzyme required for

a. Branched – chain amino acid dehydrogenase complex
b. 2 hydroxyphytanoyl caA lyase
c. Transketolase
d. All of the above

Q66. Panthothenic acid is coenzyme of which of the following reactions

a. Dehydrogenation
b. Oxidation
c. Decarbocylation
d. Reduction
e. Acetylation

Q67. Hypervitaminosis A prevent with all except

a. Hyperlipidemia
b. Alopecia
c. Pieudomer careberi
d. Hyperostosis

52. a, c	53. d	54. a	55. d	56. c	57. b	58. c	59. a	60. c	61. c
62. b	63. a	64. c	65. d	66. e	67. d			

Q68. Whole wheat is an excellent source of
a. Vitamin D b. Vitamin C
c. Vitamin A d. Thiamine

Q69. The most active form of vitamin D is
a. 25 Hydrocholecaleriferol
b. 25 Hydroyergocalcoferol
c. 24, 25 hihydroxychoecalciferol
d. 1, 25 dihydroxycholecalciferol

Q70. Tryptophan load test helps in the evaluation of deficiency of the Vitamin
a. Folic acid b. Niacinamide
c. Pyriodoxine d. cyanocobolamine

Q71. Malonic aciduria is seen in deficiency of
a. Pyridoxine b. B_{12}
C. Folic acid d. Riboflavin

Q72. Converstion of proline to hydroxyl proline is
a. Vitamin C mediated hydroxylation
b. Reverse hydroxylation
c. Inversion
d. Post translation induction

Q73. Biotin is essential for :
a. Translation b. Carboxylation
c. Hydroxylation d. Choline

Q74. A vitamin which functions as reducing agents is
a. Vitamin C b. Vitamin B_{12}
c. Thiamine d. Nicotiamide

Q75. Biotin deficiency is characterized by the following except
a. Muscular pain b. Anaemia
c. Nausea d. Dermatitis

Q76. Which vitamin is found as a constituent of Warburg yellow enzyme
a. B1 b. B2
c. Niacin d. Pantothenic acid

Q77. of prime importance in the structure of flavoproteins is
a. VitaminB_6 b. VitaminB_2
c. VitaminB_1 d. Vitamina A

Q78. Vitamin which is excreted in urine is
a. Vitamin A b. Vitamin C
c. Vitamin D d. Vitamin K

Q79. Biotin deficiency is due to
a. Avidin
b. Flavoproteins
c. Metallo flavoproteins
d. Oxireductase

Q80. Vitamin K is required for
a. Hydroxylation b. Chelation
c. Transamination d. Carboxxylation

Q81. Vitamin used in the treatment of homocystinuria is
a. B1 b. B5
c. B12 d. B6

Q82. Beta alanine is formed by
a. Biotin
b. Pyridoxal phosphate
c. Pantothenic acid
d. Folic acid

Q83. Following are seen in Vitamin A deficiency except
a. Photophobia
b. Epiphyseal defects
c. Growth retardation
d. Polyneuritis

Q84. All are true about Vitamin K except
a. Main storage organ is liver
b. Cofactor of coagaulation factor
c. Deficiency leads to Hemorrhagic disease of newborn
d. Deficiency leads to shortened PT

Q85. Which derivative of fat soluble vitamin is functioning like a hormone?
a. A b. D
c. E d. K

Q86. True statement (s) about vitamin A:
a. 1600 U retinal is used for treatment of xerophthalmia
b. >1% prevalence of night-blindness is the criteria for determining the xerophthalmia problem in the population at risk (6m-6yr)
c. Retinal is not present in milk
d. Chronic vitamin A intoxication causes papilledema

68. d	69. d	70. c	71. b	72. a	73. b	74. a	75. b	76. b	77. b
78. b	79.a	80. d	81. d	82. c	83. d	84. d	85. b	86. b, d	

Vitamins and Minerals – Explanations

1. a) Vitamin B_1

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Vitamin B_1-

Reactions catalysed by Vitamin B_1:

1. Pyruvate Dehydrogenase.
2. α ketoglutarate dehydrogenase.
3. Branched chain ketoacid dehydrogenase.
4. Transketolase reaction

Beriberi is due to deficiency of thiamine.

- Alcoholism is the most common cause of beri beri because of poor intake of B_1 and inhibition of thiamine uptake by alcohol.
- Intake of polished rice which removes the aleurone layer.

Types of beriberi:

- Wet (cardiovascular) beriberi - peripheral vasodilation → ↑ cardiac output → stimulation of Renin-Angiotensin system as vasodilation is perceived as relative loss of volume → salt and water retention → oedema.
  - Soshin beriberi – acute type of wet beriberi resulting in fulminant cardiac failure.
- Dry beriberi – Symmetric polyneuropathy, loss of deep tendon reflexes and ultimately complete paralysis
  - Wernicke encephalopathy-acute condition with ophthalmoplegia (gaze palsy), ataxia and cognitive dynfunction.
  - Korsakoff psychosis – chronic condition with anterograde amnesia, i.e., failure to convert short-term memory to long-term memory. So the patient fills the gap in memory by making up events (confabulation).
- Infantile beriberi-seen in infants of thiamine deficient mothers as their milk is devoid of thiamine.

Wernicke-Korsakoff syndrome-autosomal recessive genetic disease showing features of both Wernicke encephalopathy and Korsakoff psychosis.

Diagnosis: ↑RBC Transketolase activity after adding TDP to erythrocyte lysate in vitro.

Treatment:

- Injection of thiamine in acute stages followed by oral supplementation.
- Intravenous infusion of glucose in thiamine deficient patients should always be preceded by injection of thiamine otherwise it will precipitate or worsen symptoms.

b. Vitamin B_2-

Vitamin B_2 deficiency results in lesionsof corner of mouth, lips and tongue, seborrheic dermatitis.

c. Vitamin B_{12}-

Vitamin B_{12} deficiency causes macrocytic anemia and degeneration of the spinal cord .

d. Vitamin B_3

Vitamin B_3 is Niacin. Deficiency causes pellagra – Diarrhoea, photosensitive dermatitis, depressive psychosis .

2. c) Niacin

[Ref: Harper's Illustrated biochemistry, 29th Edition]

Niacin Is Toxic in Excess Nicotinic acid has been used to treat hyperlipidemia when of the order of 1–6 g/day are required, causing dilatation of blood vessels and flushing, along with skin irritation. Intakes of both nicotinic acid and nicotinamide in excess of 500 mg/day also cause liver damage.

3. d) Epoxide reductase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Vitamin K is the cofactor for the carboxylation of glutamate residues in the postsynthetic modification of

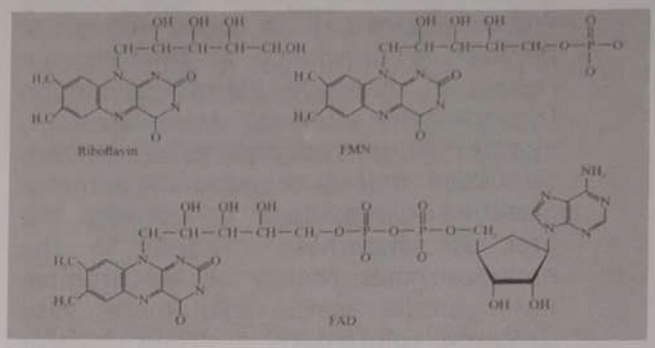
proteins to form the unusual amino acid ϒ-carboxyglutamate (Gla). Initially, vitamin K hydroquinone is oxidized to the epoxide, which activates a glutamate residue in the protein substrate to a carbanion, which reacts nonenzymatically with carbon dioxide to form ϒ-carboxyglutamate. Vitamin K epoxide is reduced to the quinone by a warfarin-sensitive reductase, and the quinone is reduced to the active hydroquinone by either the same warfarin-sensitive reductase or a warfarin-insensitive quinone reductase. In the presence of warfarin, vitamin K epoxide can-not be reduced, but accumulates and is excreted. If enough vitamin K (as the quinone) is provided in the diet, it can be reduced to the active hydroquinone by the warfarin-in-insensitive emzyme, and carboxylation can continue, with stoichiometric utilization of vitamin K and excretion of the epoxide. A high dose of vitamin K is the antidote to an overdose of warfarin.

Prothrombin and several other proteins of the blood clotting system (Factors VII, IX, and X, and proteins C and S) each contain 4 to 6 ϒ-carboxyglutamate residues. ϒ-Carboxyglutamate chelates calcium ions, and so permits the binding of the blood-clotting proteins to membranes. In vitamin K deficiency, or in the presence of warfarin, an abnormal precursor of prothrombin (preprothrombin) containing little or no ϒ-carboxyglutamate, and incapable of chelating calcium, is released into the circulation.

4. b) Vitamin B2

[Ref: Harper's Illustrated biochemistry, 30th Edition]

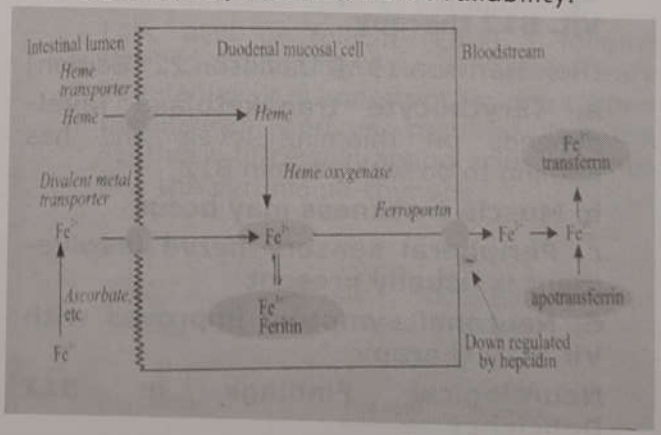
Riboflavin is centrally involved in lipid and carbohydrate metabolism, and deficiency occurs in many countries, it is not fatal, because there is very efficient conservation of tissue riboflavin. Riboflavin released by the catabolism of enzymes is rapidly incorporated into newly synthesize enzymes. Deficiency of riboflavin (vitamin B2) is characterized by cheilosis, desquamation and inflammation of the tongue, and a seborrheic dermatitis. Riboflavin nutritional status is assessed by measurement of the activation of erythrocyte glutathione reductase by FAD added in vitro.



5. b) Vitamin C

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Inorganic iron is absorbed in the FE^{2+} (reduced) state, and hence, the presence of reducing agents enhances absorption. The most effective compound is vitamin C, and while intakes of 40 to 80 mg of vitamin C per day are more than adequate to meet requirements, an intake of 25 to 50 mg per meal enhances iron absorption, especially when iron salts are used to treat iron deficiency anaemia. Alcohol and fructose also enhance iron absorption. Heme iron from is absorbed separated and is considerably more available than inorganic iron. However, the absorption of both inorganic and heme is impaired by calcium-a glass of milk with a meal significantly reduces iron availability.



6. c) Carboxylation of glutamate

a. Carboxylation of aspartate-this has no role in vitamin K in epoxide cycle

b. Dehydrogenation of glutamate- this has no role in vitamin K in epoxide cycle

c. Carboxylation of glutamate-

- Vitamin K has been known for many years to be essential for the synthesis of prothrombin and several other clotting factors. Indeed, it is called vitamin K because a deficiency in this vitamin results in defective blood koagulation (Scandinavian spelling). After ingestion, vitamin K is reduced to a dihydro derivative that is required by gamma-glutamyl carboxylase to convert the first 10 glutamate residues in the aminoterminal region of prothrombin into gamma -carboxyglutamate .Also g- carboxyglutamate, a strong chelator of Ca^{2} is required for the activation of prothrombin .
- Dicoumarol was the first anticoagulant used to prevent thromboses in patients prone to clot formation. However, it is seldom used now because of poor absorption and gastrointestinal side effects.
- Warfarin , another vitamin K antagonist, is commonlv administered as an anticoagulant. Warfarin inhibits the keto reductase and quinone reductase that are required to regenerate the dihydro derivative of vitamin K.

d. Dehydrogenation of aspartate- this has no role in vitamin K in epoxide cycle

7. b) Muscle weakness may occur
c) Peripheral sensory nerve involvement is usually present
d) Neuronal symptom improves with Vit. B12 therapy

[Ref: Harrison 19th & Davidson 22nd Edition]

a. ↓Erythocyte transketolase level- depends on thiamine levels and has nothing to do with vitamin B12

b. Muscle weakness may occur

c. Peripheral sensory nerve involvement is usually present

d. Neuronal symptom improves with Vit. B12 therapy

Neurological Findings in B12 Deficiency

Peripheral nerves

- Glove and stocking paraesthesiae
- Loss of ankle reflexes

Spinal cord

- Subacute combined degeneration of the cord

Posterior columns: diminished vibration sensation and proprioception

Corticospinal tracts: upper motor neuron signs

Cerebrum

- Dementia
- Optic atrophy

Autonomic Neuropathy

Cobalamin (Vitamin 812)

- Cobalamin deficiency may cause a bilateral peripheral neuropathy or degeneration (demyelination) of the posterior and pyramidal tracts of the spinal cord and, less frequently, optic atrophy or cerebral symptoms. The patient, more frequently male, present: with paresthesias, muscle weakness, or difficulty in walking and sometimes dementia, psychotic disturbances, or visual impairment.
- CNS involvement produces abnormal somatosensory and visual evoked potential latencies.
- The diagnosis is confirmed by finding reduced serum cobala-min levels. In upto 40% of patients, anemia and macrocytom are lacking. Serum methylmalonic acid and homocysteine, the metabolites that accumulate when cobalamin-dependent reactions are blocked. are elevated. Antibodies to intrinsic factor are present in approximately 60%, and antiparietal cell antibodies in about 90%, of individuals with pernicious anemia.
- Treatment for cobalamin deficiency usually does not completely reverse the clinical manifestations, and at least50% of patients exhibit some permanent neurologic deficit.

8. d) Alkaline phosphatase

[Ref: Textbook of Medical Biochemistry by Chatterjea and Shinde, 8th edition]

Mineral	Enzyme (Co-factor)
Iron	• Catalase • Cytochromes
Copper	• Cytochromes cytochrome oxidase • Tyrosinase • Monoamino oxidase (MAO) • Lysyl oxidase • Superoxide dismutase

Zinc	• Alcholhol dehydrogenase • Retinine reductase • Alkaline phosphatase enzyme • Glutamate dehydrogenase • Lactate dehydrogenase • DNA and RNA polymerase • ALA dehydratase
Selenium	Glutathione peroxidase

9. c) Decarboxylation

[Ref: Textbook of Medical Biochemistry by Chatterjea and Shinde, 8th edition]

Uses of Pyridoxine

Aminoacid Metabolism:

1. Transamination –AST and ALT.
2. Non oxidative Deamination – serine and threonine dehydratase.
3. Decarboxylation – histidine decarboxylase, DOPA decarboxylase and glutamate decarboxylase.
4. Transulfuration – cystathionine beta synthase and cystathioninase.

Lipid Metabolism:

1. Sphingomyelin synthesis.
2. Carnitine synthesis

Carbohydrate Metabolism:

1. Glycogenolysis – Glycogen phosphorylase.
2. Gluconeogenesis – formation of alpha keto acids.

Heme Synthesis:

1. Delta amino levulenate synthase.

10. b) Pyridoxine

Vitamin B_6 requirements

- Related to proteins intake and not to calorie intake.
- It is recommended that adults need 1 to 2 mg/day.
- To determine the requirement, plasma PLP concentration was used as the major vitamin B_6 status indicator because it best represents tissue stores.

11. a) Increases cobalamin absorption pattern

Vitamin B12 Absorption Requires Two Binding Proteins

Vitamin B12 is absorbed bound to intrinsic factor, a small glycoprotein secreted by the parietal cells of the gastric mucosa. Gastric acid and pepsin release the vitamin from protein binding in food and make it available to bind to cobalophilin, a binding protein secreted in the saliva. In the duodenum, cobalophilin is hydrolyzed, releasing the vitamin for binding to intrinsic factor. Pancreatic insufficiency can therefore be a factor in the development of vitamin B12 deficiency, resulting in the excretion of cobalophilin-bound vitamin B12. Intrinsic factor binds only the active vitamin B12 vitamers and not other corrinoids. Vitamin B12 is absorbed from the distal third of the ileum via receptors that bind the intrinsic factor-vitamin B12 complex, but not free intrinsic factor or free vitamin.

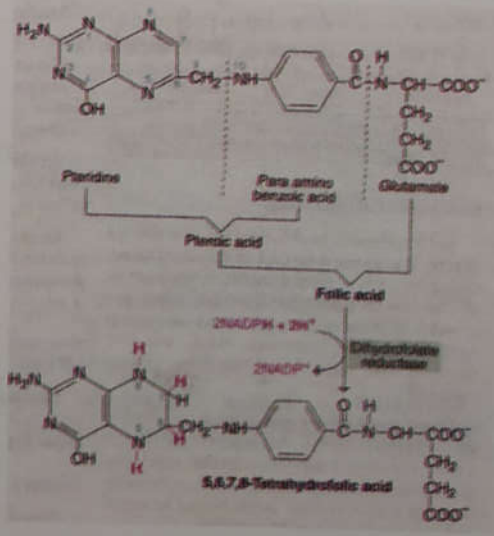
12. d) All the above

Folic acid is associated with the metabolism of histidine. Formimino-glutamate (FICLU), formed in histidine metabolism transfers the one carbon fragment, formimino group (-CH=NH) to tetrahydrofolate to produce N5-formimino THF. In case of folic acid deficiency, FIGLU accumulates and is excreted in urine. Histidine load test utilizing the excretion of FIGLU in urine is used to assess folic acid deficiencv.

13. c) Alanine

[Ref: Satyanarayan 4th Edition]

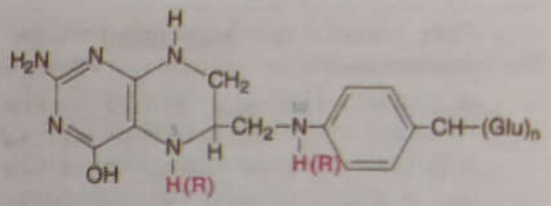
Folic acid or folacin (Latin : folium-leaf) is abundantly found in green leafy vegetables. It is important for one carbon metabolism and is required for the synthesis of certain amino acids, purines and the pyrimidine-thymine.



Biochemical functions

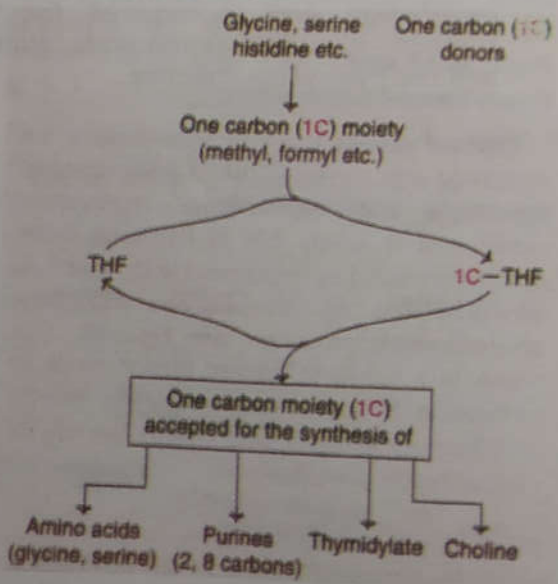
Tetrahydrofolate (THF), the coenzyme of folic acid, is actively involved in the one carbon metabolism. THF serves as an acceptor or donor of one carbon units (formyl, methyl etc.) in a variety of reactions involving amino acid and nucleotide metabolism.

The one carbon units bind with THF at position at N5 or N10 or on both N5 and N10 of pteroyl structure. The attachment of formyl (-CHO) at position 5 of THF gives N5-formyl tetrahydrofolate which is commonly known as folinic acid or citrovorum factor. The other commonly found one carbon moieties and their binding with THF are given below.



THF-1 carbon derivative	R group (one carbon unit)
N^5-Formyl THF	–CHO
N^{10}-Formyl THF	–CHO
N^5-Formimino THF	–CH=NH
N^5, N^{10}-Methenyl THF	≡CH
N^5, N^{10}-Methylene THF	=CH_2
N^5 – Methyl THF	–CH_3

The essential functions of THF in one carbon metabolism



An overview of one carbon metabolism

14. c) Selenium

Free radicals are formed in the body under normal conditions. They cause damage to nucleic acids, proteins, and lipids in cell membranes and plasma lipoproteins. This can cause cancer, atherosclerosis and coronary artery disease, and auto-immune diseases. Epidemiological and laboratory studies have identified a number of protective antioxidant nutrients: selenium, vitamins C and E, β-carotene, and a variety of polyphenolic compounds derived from plant foods. Many people take supplements of one or more antioxidant nutrients.

The peroxides that are formed by radical damage to lipids in membranes and plasma lipoproteins are reduced to fatty acids by glutathione peroxidase, a selenium-dependent enzyme (hence the importance of adequate selenium intake to maximize antioxidant activity), and the oxidized glutathione is reduced by NADPH-dependent glutathione reductase.

15. b) Cu

Ceruloplasmin (contains Cu2+; albumin probably more important in physiologic transport of Cu2+)

Ceruloplasmin (about 160 kDa) is an α2-globulin. It has a blue color because of its high copper content and carries 90% of the copper present in plasma. Each molecule of ceruloplasmin binds six atoms of copper very tightly, so that the copper is not readily exchangeable. Albumin carries the other ~10% of the plasma copper, but binds the metal less tightly than does ceruloplasmin. Albumin thus donates its copper to tissues more readily than ceruloplasmin and appears to be more important than ceruloplasmin in copper transport in the human body. Ceruloplasmin exhibits a copper-dependent oxidase activity, but its physiologic significance has not been clarified apart from possible involvement in the oxidation of Fe2+ in transferrin to Fe3+. The amount of ceruloplasmin in plasma is decreased in liver disease. In particular, low levels of ceruloplasmin are

found in Wilson disease (hepatolenticular degeneration), a disease due to abnormal metabolism of copper. In order to clarify the description of Wilson disease, we shall first consider the metabolism of copper in the human body and then Menkes disease, another condition involving abnormal copper metabolism.

16. d) Spleen

[Ref: Harper's Illustrated Biochemistry, 29th edition]

Wilson Disease Is Also Due to Mutations in a Gene Encoding a Copper-Binding P-Type ATPase

Wilson disease is a genetic disease in which copper fails to be excreted in the bile and accumulates in liver, brain, kidney, and red blood cells. It can be regarded as an inability to maintain a near-zero copper balance, resulting in copper toxicosis. The increase of copper in liver cells appears to inhibit the coupling of copper to apoceruloplasmin and leads to low levels of ceruloplasmin in plasma. As the amount of copper accumulates, patients may develop a hemolytic anemia, chronic liver disease (cirrhosis, hepatitis), and a neurologic syndrome owing to accumulation of copper in the basal ganglia and other centers. A frequent clinical finding is the Kayser-Fleischer ring. This is a green or golden pigment ring around the cornea due to deposition of copper in Descemet's membrane.

Major Laboratory Tests Used in the Investigation of Diseases of Copper Metabolism

Test	Normal Adult Range
Serum copper	10-22 μμολ/Λ
Ceruloplasmin	200-600 mg/L
Urinary copper	<1 μμολ/24η
Liver copper	20-50 μγ/γ δρψ ωειγητ

If Wilson disease is suspected, a liver biopsy should be performed; a value for liver copper of over 250 μg/g dry weight along with a plasma level of ceruloplasmin of under 20 mg/dL is diagnostic, the accumulation of copper in liver and subsequently in other organs such as brain.

17. b) Molybdenum

xanthine oxidase, which contains molybdenum and plays an important role in the conversion of purine bases to uric acid, and is of particular significance in uricotelic animals ; and aldehyde dehydrogenase, an FAD-linked enzyme present in mammalian livers, which contains molybdenum and nonheme iron and acts upon aldehydes and N-heterocyclic substrates. The mechanisms of oxidation and reduction of these enzymes are complex.

18. b) Cu

Collagen Undergoes Extensive Posttranslational Modifications Newly synthesized collagen undergoes extensive posttranslational modification before becoming part of a mature extracellular collagen fiber .Like most secreted proteins, collagen is synthesized on ribosomes in a precursor form, preprocollagen, which contains a leader or signal sequence that directs the polypeptide chain into the lumen of the endoplasmic reticulum. As it enters the endoplasmic reticulum, this leader sequence is enzymatically removed.

Self-assembly is a cardinal principle in the biosynthesis of collagen. Following secretion from the cell by way of the Golgi apparatus, extracellular enzymes called procollagen aminoproteinase and procollagen carboxyproteinase remove the extension peptides at the amino and carboxyl terminal ends, respectively. Cleavage of these propeptides may occur within crypts or folds in the cell membrane. Once the propeptides are removed, the triple helical collagen molecules, containing approximately 1000 amino acids per chain, spontaneously assemble into collagen fibers. These are further stabilized by the formation of inter- and intrachain cross-links through the action of lysyl oxidase requires copper.

19. a) Copper

Cytochrome oxidase is a hemoprotein widely distributed in many tissues,

having the typical heme prosthetic group present in myoglobin, hemoglobin, and other cytochromes . It is the terminal component of the chain of respiratory carriers found in mitochondria and transfers electrons resulting from the oxidation of substrate molecules by dehydrogenases to their final acceptor, oxygen. The enzyme is poisoned by carbon monoxide, cyanide, and hydrogen sulfide. It has also been termed "cytochrome a3." However, it is now known that the heme a3 is combined with another heme, heme a, in a single protein to form the cytochrome oxidase enzyme complex and so it is more correctly termed cytochrome aa3. It contains two molecules of heme, each having one Fe atom that oscillates between Fe3+ and Fe2+ during oxidation and reduction. Furthermore, two atoms of Cu are present, each associated with a heme unit.

20. b) Cu

Collagen types that form long rod-like fibers in tissues are assembled by lateral association of these triple helical units into a "quarter staggered" alignment such that each is displaced longitudinally from its neighbor by slightly less than one-quarter of its length . This arrangement is responsible for the banded appearance of these fibers in connective tissues. Collagen fibers are further stabilized by the formation of covalent cross-links, both within and between the triple helical units. These cross-links form through the action of lysyl oxidase, a copper-dependent enzyme that oxidatively deaminates the ε-amino groups of certain lysine and hydroxylysine residues, yielding reactive aldehydes. Such aldehydes can form aldol condensation products with other lysine- or hydroxylysine-derived aldehydes or form Schiff bases with the ε-amino groups of unoxidized lysines or hydroxylysines. These reactions, after further chemical rearrangements, result in the stable covalent cross-links that are important for the tensile strength of the fibers. Histidine may also be involved in certain cross-links. Several collagen types do not form fibrils in tissues . They are characterized by interruptions of the triple helix with stretches of protein lacking Gly-X-Y repeat sequences. These non-Gly-X-Y sequences result in areas of globular structure interspersed in the triple helical structure. Type IV collagen, the best-characterized example of a collagen with discontinuous triple helices, is an important component of basement membranes, where it forms a mesh like network.

21. c) Beriberi

Thiamin Deficiency Affects the Nervous System & the Heart Thiamin deficiency can result in three distinct syndromes: a chronic peripheral neuritis, beriberi, which may or may not be associated with heart failure and edema; acute pernicious (fulminating) beriberi (shoshin beriberi), in which heart failure and metabolic abnormalities predominate, without peripheral neuritis; and Wernicke encephalopathy with Korsakoff psychosis, which is associated especially with alcohol and narcotic abuse. The role of thiamin diphosphate in pyruvate dehydrogenase means that in deficiency there is impaired conversion of pyruvate to acetyl CoA. In subjects on a relatively high carbohydrate diet, this results in increased plasma concentrations of lactate and pyruvate, which may cause lifethreatening lactic acidosis.

22. b) Transketolase activity

Thiamin Nutritional Status Can Be Assessed by Erythrocyte Transketolase Activation The activation of apo-transketolase (the enzyme protein) in erythrocyte lysate by thiamin diphosphate added in vitro has become the accepted index of thiamin nutritional status.

23. b) Riboflavin

Riboflavin Deficiency Is Widespread but Not Fatal Although riboflavin is centrally involved in lipid and carbohydrate metabolism, and deficiency occurs in many countries, it is not fatal, because there is very efficient conservation of tissue riboflavin. Riboflavin released by the catabolism of enzymes is rapidly incorporated into newly synthesized

enzymes. Deficiency is characterized by cheilosis, desquamation and inflammation of the tongue, and a seborrheic dermatitis. Riboflavin nutritional status is assessed by measurement of the activation of erythrocyte glutathione reductase by FAD added in vitro.

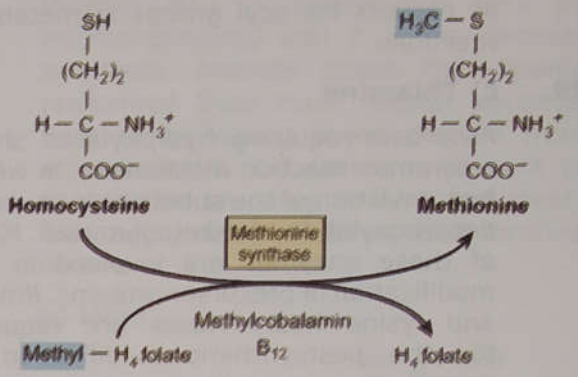
24. a) Folic acid

Tetrahydrofolate Is a Carrier of One-Carbon Units Tetrahydrofolate can carry one-carbon fragments attached to N-5 (formyl, formimino, or methyl groups), N-10 (formyl) or bridging N-5–N-10 (methylene or methenyl groups). 5-Formyl-tetrahydrofolate is more stable than folate, and is therefore used pharmaceutically (known as folinic acid), and the synthetic (racemic) compound (leucovorin). The major point of entry for one-carbon fragments into substituted folates is methylene-tetrahydrofolate , which is formed by the reaction of glycine, serine, and choline with tetrahydrofolate. Serine is the most important source of substituted folates for biosynthetic reactions, and the activity of serine hydroxymethyltransferase is regulated by the state of folate substitution and the availability of folate. The reaction is reversible, and in liver it can form serine from glycine as a substrate for gluconeogenesis. Methylene-, methenyl-, and 10-formyl-tetrahydrofolates are interconvertible. When onecarbon folates are not required, the oxidation of formyl-tetrahydrofolate to yield carbon dioxide provides a means of maintaining a pool of free folate.

25. b) Homocysteine to methionine

[Ref: Harper's Illustrated Biochemistry, 29th edition]

There Are Three Vitamin B12– Dependent Enzymes Methylmalonyl CoA mutase, leucine aminomutase, and methionine synthase are vitamin B12–dependent enzymes. Methylmalonyl CoA is formed as an intermediate in the catabolism of valine and by the carboxylation of propionyl CoA arising in the catabolism of isoleucine, cholesterol, and, rarely, fatty acids with an odd number of carbon atoms or directly from propionate, a major product of microbial fermentation in the rumen. It undergoes a vitamin B12–dependent rearrangement to succinyl CoA, catalyzed by methylmalonyl CoA mutase . The activity of this enzyme is greatly reduced in vitamin B12 deficiency, leading to an accumulation of methylmalonyl CoA and urinary excretion of methylmalonic acid, which provides a means of assessing vitamin B12 nutritional status.



Homocysteine and the "folate trap." Vitamin B12 deficiency leads to impairment of methionine synthase, resulting in accumulation of homocysteine and trapping folate as methyltetrahydrofolate.

26. c) Pyrdoxine

Vitamin B6 Has Several Roles in Metabolism Pyridoxal phosphate is a coenzyme for many enzymes involved in amino acid metabolism, especially transamination and decarboxylation. It is also the cofactor of glycogen phosphorylase, where the phosphate group is catalytically important. In addition, B6 is important in steroid hormone action. Pyridoxal phosphate removes the hormone-receptor complex from DNA binding, terminating the action of the hormones. In vitamin B6 deficiency, there is increased sensitivity to the actions of low concentrations of estrogens, androgens, cortisol, and vitamin D.

27. b) Xanthurenic acid

Vitamin B6 Deficiency Is Rare

Although clinical deficiency disease is rare, there is evidence that a significant proportion of the population have marginal vitamin B6 status. Moderate deficiency results in abnormalities of tryptophan

and methionine metabolism. Increased sensitivity to steroid hormone action may be important in the development of hormone-dependent cancer of the breast, uterus, and prostate, and vitamin B6 status may affect the prognosis.

28. a) Pantothenic group

Pantothenic acid is present in coenzyme A and acyl carrier protein, which act as carriers for acyl groups in metabolic reactions.

29. c) Thiamine

Ascorbate-requiring hydroxylases share a common reaction mechanism, in which hydroxylation of the substrate is linked to decarboxylation of α-ketoglutarate. Many of these enzymes are involved in the modification of precursor proteins. Proline and lysine hydroxylases are required for the postsynthetic modification of procollagen to collagen, and proline hydroxylase is also required in formation of osteocalcin and the C1q component of complement.

30. b) Thiamine

thiamin participates in decarboxylation of α-keto acids, The decarboxylation requires Mg++ or Mn++ ions.

thiamin (vitamin B1), as thiamin diphosphate, the coenzyme for decarboxylation in the α-ketoglutarate dehydrogenase reaction.

31. c) 1 hydroxylation of vitamin D

Skin

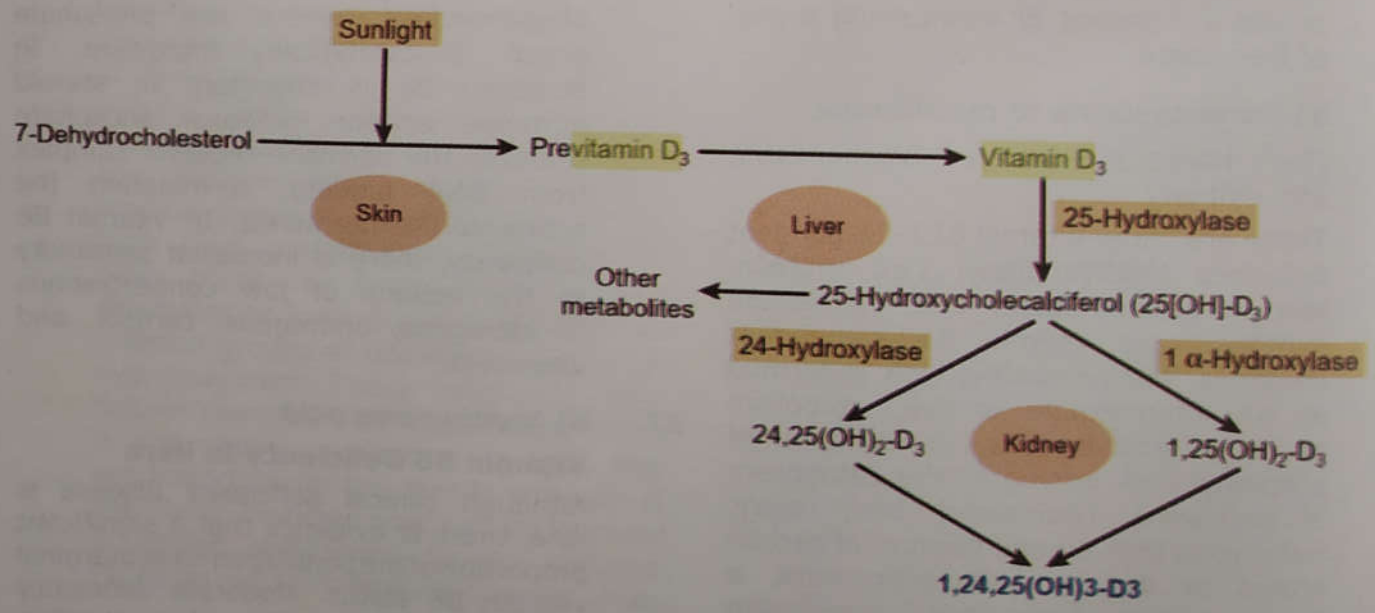
Small amounts of the precursor for 1,25(OH)2-D3 synthesis are present in food (fish liver oil, egg yolk), but most of the precursor for 1,25(OH)2-D3 synthesis is produced in the malpighian layer of the epidermis from 7-dehydrocholesterol in an ultraviolet light-mediated, nonenzymatic photolysis reaction.

Liver

A specific transport protein called the vitamin D–binding protein binds vitamin D3 and its metabolites and moves vitamin D3 from the skin or intestine to the liver, where it undergoes 25-hydroxylation, the first obligatory reaction in the production of 1,25(OH)2-D3.

Kidney

25(OH)2-D3 is a weak agonist and must be modified by hydroxylation at position C1 for full biologic activity. This is accomplished in mitochondria of the renal proximal convoluted tubule by a three-component monooxygenase reaction that requires NADPH, Mg2+, molecular oxygen, and at least three enzymes: (1) a flavoprotein, renal ferredoxin reductase; (2) an iron sulfur protein, renal ferredoxin; and (3) cytochrome P450. This system produces 1,25(OH)2-D3, which is the most potent naturally occurring metabolite of vitamin D.



32. c) Millets

Pellagra Is Caused by Deficiency of Tryptophan & Niacin Pellagra is characterized by a photosensitive dermatitis.Although the nutritional etiology of pellagra is well established, and tryptophan or niacin prevents or cures the disease, additional factors, including deficiency of riboflavin or vitamin B6, both of which are required for synthesis of nicotinamide from tryptophan, may be important.

33. c) Microcytic anemia

Vitamin B12 Deficiency Causes Pernicious Anemia Pernicious anemia arises when vitamin B12 deficiency impairs the metabolism of folic acid, leading to functional folate deficiency that disturbs erythropoiesis, causing immature precursors of erythrocytes to be released into the circulation (megaloblastic anemia). The most common cause of pernicious anemia is failure of the absorption of vitamin B12 rather than dietary deficiency. This can be the result of failure of intrinsic factor secretion caused by autoimmune disease affecting parietal cells or from production of anti-intrinsic factor antibodies. There is irreversible degeneration of the spinal cord in pernicious anemia, as a result of failure of methylation of one arginine residue on myelin basic protein. This is the result of methionine deficiency in the central nervous system, rather than secondary folate deficiency.

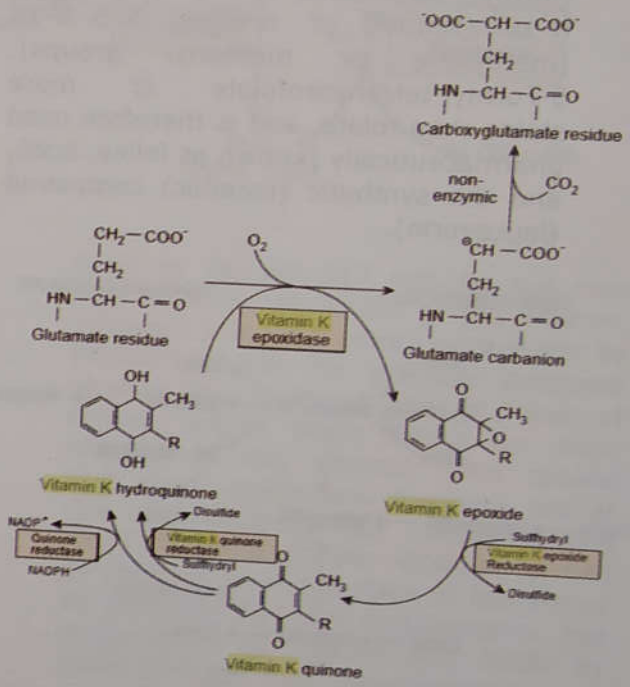
34. d) K and B

A true vitamin K deficiency is unusual because adequate amounts are generally produced by intestinal bacteria or obtained from the diet. If the bacterial population in the gut is decreased (for example, by antibiotics), the amount of endogenously formed vitamin is depressed, and this can lead to hypoprothrombinemia in the marginally malnourished individual (for example, a debilitated geriatric patient). This condition may require supplementation with vitamin K to correct the bleeding tendency. In addition, certain second-generation cephalosporin antibiotics (for example, cefamandole) cause hypoprothrombinemia, apparently by a warfarin-like mechanism that inhibits VKOR. Consequently, their use in treatment is usually supplemented with vitamin K.

Vitamin B1 ,b2 ,b12 ,b7 are synthesized by intestinal Bacteria.

Vitamin B12 is synthesized only by microorganisms, and it is not present in plants. Animals obtain the vitamin preformed from their natural bacterial flora or by eating foods derived from other animals. Cobalamin is present in appreciable amounts in liver, red meat, fish, eggs, dairy products, and fortified cereals.

35. a) Liver



The role of vitamin K in the synthesis of γ-carboxyglutamate.
Occurs in liver

36. b) Glutathione reductase

Riboflavin Deficiency Is Widespread but Not Fatal

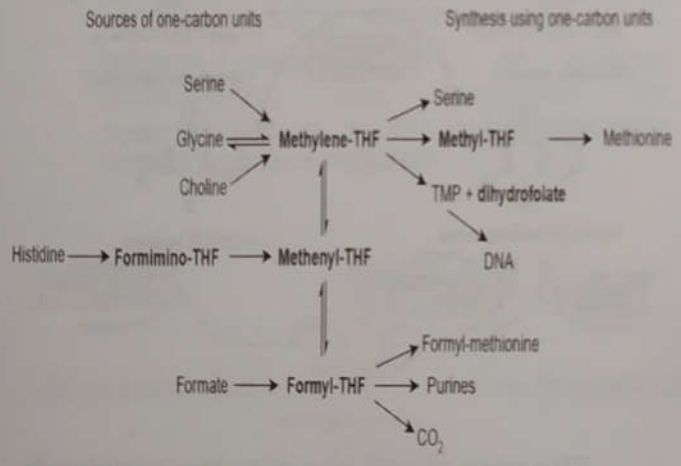
Although riboflavin is centrally involved in lipid and carbohydrate metabolism, and deficiency occurs in many countries,

it is not fatal, because there is very efficient conservation of tissue riboflavin. Riboflavin released by the catabolism of enzymes is rapidly incorporated into newly synthesized enzymes. Deficiency is characterized by cheilosis, desquamation and inflammation of the tongue, and a seborrheic dermatitis. Riboflavin nutritional status is assessed by measurement of the activation of erythrocyte glutathione reductase by FAD added in vitro.

37. a) Methylene THF

[Ref: Harper's Illustrated Biochemistry, 29th edition]

Tetrahydrofolate Is a Carrier of One-Carbon Units Tetrahydrofolate can carry one-carbon fragments attached to N-5 (formyl, formimino, or methyl groups), N-10 (formyl) or bridging N-5–N-10 (methylene or methenyl groups). 5-Formyl-tetrahydrofolate is more stable than folate, and is therefore used pharmaceutically (known as folinic acid), and the synthetic (racemic) compound (leucovorin).



38. d) Riboflavin

Vitamin b2 (riboflavin) has a central role in energy-yielding metabolism

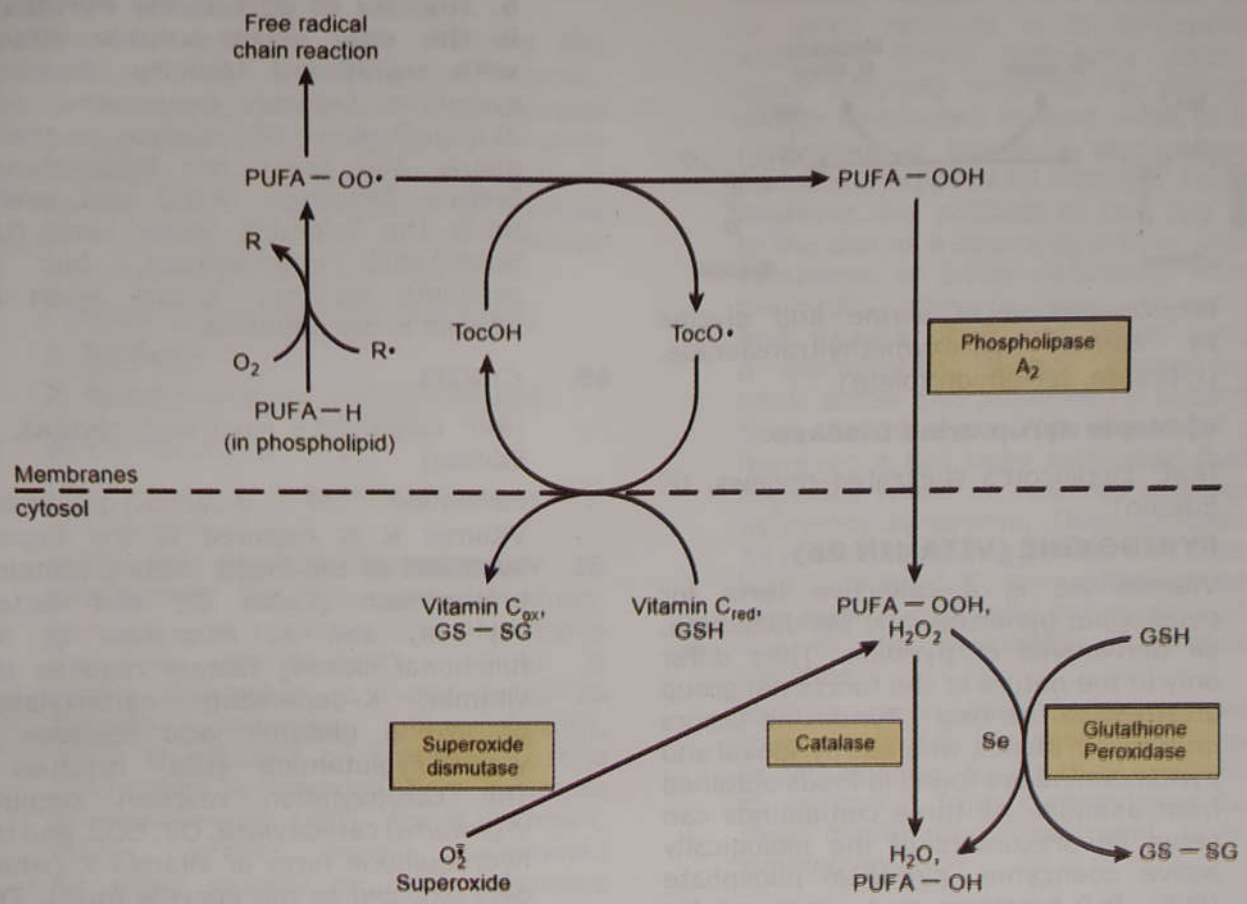
Riboflavin provides the reactive moieties of the coenzymes flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) . FMN is formed by ATP-dependent phosphorylation of riboflavin, whereas FAD is synthesized by further reaction with ATP in which its AMP moiety is transferred to FMN. The main dietary sources of riboflavin are milk and dairy products. In addition, because of its intense yellow color, riboflavin is widely used as a food additive.

Flavin Coenzymes Are Electron Carriers in Oxidoreduction Reactions These include the mitochondrial respiratory chain, key enzymes in fatty acid and amino acid oxidation, and the citric acid cycle. Reoxidation of the reduced flavin in oxygenases and mixed-function oxidases proceeds by way of formation of the flavin radical and flavin hydroperoxide, with the intermediate generation of superoxide and perhydroxyl radicals and hydrogen peroxide. Because of this, flavin oxidases make a significant contribution to the total oxidant stress in the body.

39. d) Protection of Biological membrane from free radical damage

[Ref: Harper's Illustrated Biochemistry, 29th edition]

Vitamin E Is the Major Lipid-Soluble Antioxidant in Cell Membranes and Plasma Lipoproteins The main function of vitamin E is as a chain-breaking, freeradical-trapping antioxidant in cell membranes and plasma lipoproteins by reacting with the lipid peroxide radicals formed by peroxidation of polyunsaturated fatty acid. The tocopheroxyl radical product is relatively unreactive, and ultimately forms nonradical compounds. Commonly, the tocopheroxyl radical is reduced back to tocopherol by reaction with vitamin C from plasma . The resultant monodehydroascorbate radical then undergoes enzymic or nonenzymic reaction to yield ascorbate and dehydroascorbate, neither of which is a radical.



40. a) Vitamin B6

In Excess, Vitamin B6 Causes Sensory Neuropathy The development of sensory neuropathy has been reported in patients taking 2–7 g of pyridoxine per day for a variety of reasons (there is some slight evidence that it is effective in treating premenstrual syndrome). There was some residual damage after withdrawal of these high doses; other reports suggest that intakes in excess of 200 mg/d are associated with neurologic damage.

41. a) Cobalamine

Vitamin B12 is found only in foods of animal origin

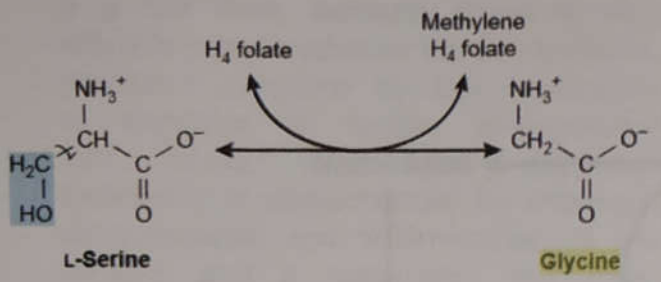
The term "vitamin B12" is used as a generic descriptor for the cobalamins—those corrinoids (cobalt-containing compounds possessing the corrin ring) having the biologic activity of the vitamin. Some corrinoids that are growth factors for microorganisms not only have no vitamin B12 activity, but may also be anti-metabolites of the vitamin. Although it is synthesized exclusively by microorganisms, for practical purposes vitamin B12 is found only in foods of animal origin, there being no plant sources of this vitamin. This means that strict vegetarians (vegans) are at risk of developing B12 deficiency. The small amounts of the vitamin formed by bacteria on the surface of fruits may be adequate to meet requirements, but preparations of vitamin B12 made by bacterial fermentation are available.

42. a) Folic acid

43. c) Niacin

[Ref: Harper's Illustrated biochemistry, 29th Edition]

Serine Following conversion to glycine, catalyzed by serine hydroxyl methyl transferase, serine catabolism merges with that of glycine.



Interconversion of serine and glycine by serine hydroxymethyltransferase. (H4folate, tetrahydrofolate)

44. c) Maple syrup urine Disease

[Ref: Lippincott's illustrated reviews, 6th Edition]

PYRIDOXINE (VITAMIN B6)

Vitamin B6 is a collective term for pyridoxine, pyridoxal, and pyridoxamine, all derivatives of pyridine. They differ only in the nature of the functional group attached to the ring . Pyridoxine occurs primarily in plants, whereas pyridoxal and pyridoxamine are found in foods obtained from animals. All three compounds can serve as precursors of the biologically active coenzyme, pyridoxal phosphate (PLP). PLP functions as a coenzyme for a large number of enzymes, particularly those that catalyze reactions involving amino acids, for example, in the synthesis of cysteine from Hcy . [Note: PLP is also required by glycogen phosphorylase.]

Reaction type	Example
Transamination	Oxaloacetate + glutamate ⇄ aspartate + α-ketoglutarate
Deamination	Serine → pyruvate + NH_3
Decarboxylation	Histidine → histamine + CO_2
Condensation	Glycine + succinyl CoA → δ-aminolevulinic acid

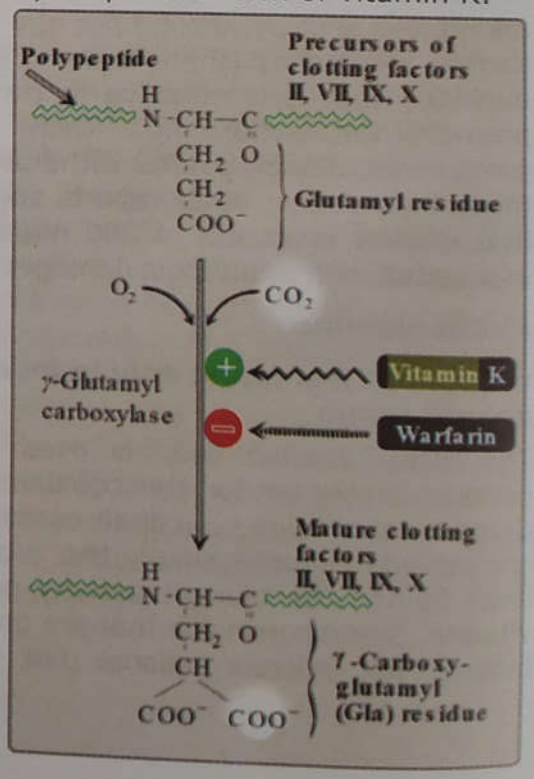
a. Clinical indications for pyridoxine Isoniazid, a drug commonly used to treat tuberculosis, can induce a vitamin B6 deficiency by forming an inactive derivative with PLP. Dietary supplementation with B6 is, thus, an adjunct to isoniazid treatment. Otherwise, dietary deficiencies in pyridoxine are rare but have been observed in newborn infants fed formulas low in B6, in women taking oral contraceptives, and in alcoholics.

b. Toxicity of pyridoxine Pyridoxine is the only water-soluble vitamin with significant toxicity. Neurologic symptoms (sensory neuropathy) occur at intakes above 500 mg/day, an amount nearly 400 times the Recommended Dietary Allowance (RDA) and over 5 times the Tolerable Upper Limit (UL). Substantial improvement, but not complete recovery, occurs when the vitamin is discontinued.

45. c) VIII

[Ref: Lippincott's illustrated reviews, 6th Edition]

Formation of γ-carboxyglutamate: Vitamin K is required in the hepatic synthesis of the blood clotting proteins, prothrombin (factor II) and factors VII, IX, and X. Formation of the functional clotting factors requires the vitamin K–dependent carboxylation of several glutamic acid residues to γ-carboxyglutamate (Gla) residues . The carboxylation reaction requires γ-glutamyl carboxylase, O2, CO2, and the hydroquinone form of vitamin K (which gets oxidized to the epoxide form). The formation of Gla residues is sensitive to inhibition by warfarin, a synthetic analog of vitamin K that inhibits vitamin K epoxide reductase (VKOR), the enzyme required to regenerate the functional hydroquinone form of vitamin K.



46. b) Homocystinemia

Thiamine pyrophosphate (TPP) is the biologically active form of the vitamin, formed by the transfer of a pyrophosphate group from adenosine triphosphate (ATP) to thiamine . TPP serves as a coenzyme in the formation or degradation of α-ketols by transketolase , and in the oxidative decarboxylation of α-keto acids.

Clinical indications for thiamine:

1. Beriberi

2. Wernicke-Korsakoff syndrome

47. d) Carboxylase

[Ref: Harper's Illustrated Biochemistry, 29th edition]

DIETARY BIOTIN DEFICIENCY IS UNKNOWN The structures of biotin, biocytin, and carboxybiotin (the active metabolic intermediate) . Biotin is widely distributed in many foods as biocytin (ε-amino- biotinyllysine), which is released on proteolysis. It is synthesized by intestinal flora in excess of requirements. Deficiency is unknown, except among people maintained for many months on total parenteral nutrition, and a very small number who eat abnormally large amounts of uncooked egg white, which contains avidin, a protein that binds biotin and renders it unavailable for absorption.

Biotin Is a Coenzyme of Carboxylase Enzymes Biotin functions to transfer carbon dioxide in a small number of reactions: acetyl-CoA carboxylase, pyruvate carboxylase , propionyl-CoA carboxylase , and methylcrotonyl-CoA carboxylase. A holocarboxylase synthetase catalyzes the transfer of biotin onto a lysine residue of the apo-enzyme to form the biocytin residue of the holoenzyme. The reactive intermediate is 1-N-carboxy-biocytin, formed from bicarbonate in an ATP-dependent reaction. The carboxy group is then transferred to the substrate for carboxylation. Biotin also has a role in regulation of the cell cycle, acting to biotinylate key nuclear proteins.

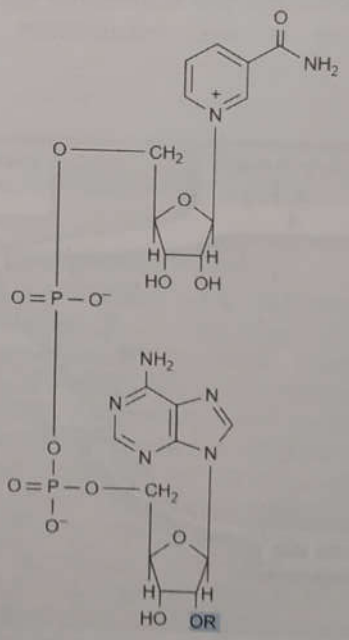
48. a) Biotin

Biotin is a coenzyme in carboxylation reactions, in which it serves as a carrier of activated carbon dioxide. Biotin is covalently bound to the ε-amino group of lysine residues in biotin-dependent enzymes. Biotin deficiency does not occur naturally because the vitamin is widely distributed in food. Also, a large percentage of the biotin requirement in humans is supplied by intestinal bacteria. However, the addition of raw egg white to the diet as a source of protein induces symptoms of biotin deficiency, namely, dermatitis, glossitis, loss of appetite, and nausea. Raw egg white contains a glycoprotein, avidin, which tightly binds biotin and prevents its absorption from the intestine. With a normal diet, however, it has been estimated that 20 eggs/day would be required to induce a deficiency syndrome. Thus, inclusion of an occasional raw egg in the diet does not lead to biotin deficiency, although eating raw eggs is generally not recommended due to the possibility of salmonella infection.

Multiple carboxylase deficiency results from a defect in the ability to add biotin to carboxylases during their synthesis or to remove it from carboxylases during their degradation. Treatment is biotin supplementation.

49. c) Tryptophan

Nicotinamide is a component of the redox coenzymes NAD and NADP,



Structure of NAD+ and NADP+. For NAD+, R = H. For NADP+, R = PO32−.

50. c) B3

[Ref: Harper's Illustrated biochemistry, 29th Edition]

Niacin is not strictly a vitamin Niacin was discovered as a nutrient during studies of pellagra. It is not strictly a vitamin since it can be synthesized in the body from the essential amino acid tryptophan. Two compounds, nicotinic acid and nicotinamide, have the biologic activity of niacin; its metabolic function is as the nicotinamide ring of the coenzymes NAD and NADP in oxidation/reduction reactions . Some 60 mg of tryptophan is equivalent to 1 mg of dietary niacin. The niacin content of foods is expressed as:

mg Niacin equivalents = mg Preformed niacin + 1/60 × mg Tryptophan

Because most of the niacin in cereals is biologically unavailable, this is discounted.

51. b) Tryptophan

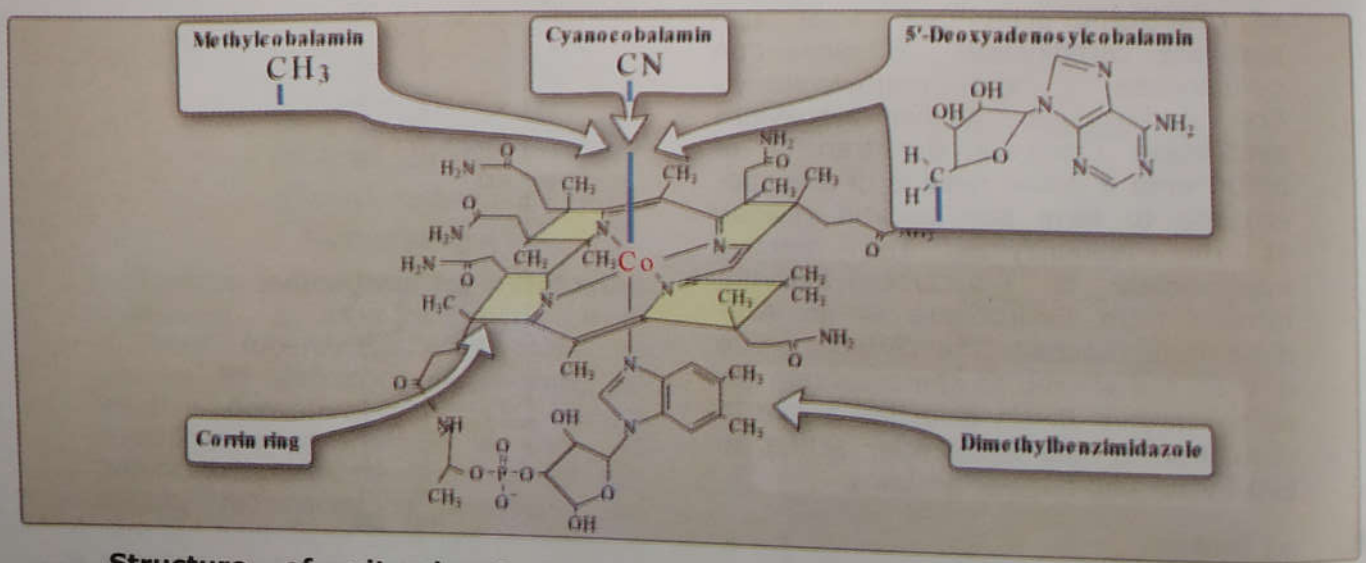
Pellagra Is Caused by Deficiency of Tryptophan & Niacin

Pellagra is characterized by a photosensitive dermatitis. As the condition progresses, there is dementia and possibly diarrhea. Untreated pellagra is fatal. Although the nutritional etiology of pellagra is well established, and tryptophan or niacin prevents or cures the disease, additional factors, including deficiency of riboflavin or vitamin B6, both of which are required for synthesis of nicotinamide from tryptophan, may be important. In most outbreaks of pellagra, twice as many women as men are affected, probably the result of inhibition of tryptophan metabolism by estrogen metabolites.

52. a) Extrinsic factor of castle
c) Cyanocbalamine

[Ref: Lippincott's illustrated reviews, 6th Edition]

Cobalamin contains a corrin ring system that resembles the porphyrin ring of heme , and but differs in that two of the pyrrole rings are linked directly rather than through a methene bridge. Cobalt is held in the center of the corrin ring by four coordination bonds with the nitrogens of the pyrrole groups. The remaining coordination bonds of the cobalt are with the nitrogen of 5,6-dimethylbenzimidazole and with cyanide in commercial preparations of the vitamin in the form of cyanocobalamin. The physiologic coenzyme forms of cobalamin are 5′-deoxyadenosylcobalamin and methylcobalamin, in which cyanide is replaced with 5′-deoxyadenosine or a methyl group, respectively.



Structure of vitamin B12 (cyanocobalamin) and its coenzyme forms (methylcobalamin and 5′-deoxyadenosylcobalamin).

53. d) Adrenal cortex

[Ref: Lippincott's illustrated reviews, 6th Edition]

Ascorbic acid (vitamin C)

The active form of vitamin C is ascorbic acid . The main function of ascorbate is as a reducing agent in several different reactions. Vitamin C has a well-documented role as a coenzyme in hydroxylation reactions (for example, hydroxylation of prolyl and lysyl residues of collagen). Vitamin C is, therefore, required for the maintenance of normal connective tissue as well as for wound healing. Vitamin C also reduces ferric iron to the ferrous form, thereby facilitating the absorption of dietary iron from the intestine.

A. Deficiency of ascorbic acid A deficiency of ascorbic acid results in scurvy, a disease characterized by sore and spongy gums, loose teeth, fragile blood vessels, swollen joints, fatigue, and a microcytic anemia caused by decreased absorption of iron. Many of the deficiency symptoms can be explained by a deficiency in the hydroxylation of collagen, resulting in defective connective tissue.

B. Prevention of chronic disease Vitamin C is one of a group of nutrients that includes vitamin E and β-carotene which are known as antioxidants. [Note: Ascorbate regenerates the functional, reduced form of vitamin E.] Consumption of diets rich in these compounds is associated with a decreased incidence of some chronic diseases, such as coronary heart disease and certain cancers. However, clinical trials involving supplementation with the isolated antioxidants have failed to demonstrate any convincing beneficial effects.

54. a) Biotin

Multiple carboxylase deficiency results from a defect in the ability to add biotin to carboxylases during their synthesis or to remove it from carboxylases during their degradation. Treatment is biotin supplementation.

55. d) It is coenzyme for pyruvate dehydrogenase and alpha ketoglutarte dehydrogense

[Ref: Lippincott's illustrated reviews, 6th Edition]

Vitamin B_1	Thiamine	Thiamine pyrophosphate	Coenzyme of enzymes catalyzing: Pyruvate → acetyl CoA α- Ketoglutarate → Συχχινψλ ΧοΑ Ριβοσε 5–Π + ξψλυλοσε 5–Π → Sedoheptulose 7-P + Glyceraldehyde 3-P Branched-chain α-ke to acid ocidation

56. c) Glutamate

VITAMIN K

The principal role of vitamin K is in the posttranslational modification of a number of proteins (most of which are involved with blood clotting), in which it serves as a coenzyme in the carboxylation of certain glutamic acid residues present in these proteins. Vitamin K exists in several forms, for example, in plants as phylloquinone (or vitamin K1), and in intestinal bacterial flora as menaquinone (or vitamin K2). A synthetic form of vvitamin K, menadione, is able to be converted to K2.

Function of vitamin K

1. Formation of γ-carboxyglutamate: Vitamin K is required in the hepatic synthesis of the blood clotting proteins, prothrombin (factor II) and factors VII, IX, and X. Formation of the functional clotting factors requires the vitamin K–dependent carboxylation of several glutamic acid residues to γ-carboxyglutamate (Gla) residues . The carboxylation reaction requires γ-glutamyl carboxylase, O2, CO2, and the hydroquinone form of vitamin K (which gets oxidized to the epoxide form). The formation of Gla residues is sensitive to inhibition by warfarin, a synthetic analog of vitamin K that inhibits vitamin

K epoxide reductase (VKOR), the enzyme required to regenerate the functional hydroquinone form of vitamin K.

EXTRA EDGE:

Toxicity of vitamin K

Prolonged administration of large doses of synthetic vitamin K (menadione) can produce hemolytic anemia and jaundice in the infant, due to toxic effects on the membrane of RBCs. Therefore, it is no longer used to treat vitamin K deficiency. No UL has been set for vitamin K.

57. b) Folic acid

[Ref: Lippincott's illustrated reviews, 6th Edition]

FOLIC ACID

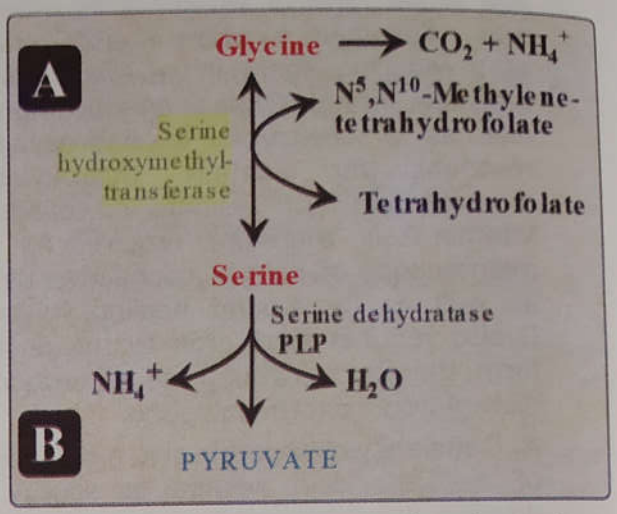
Folic acid (or folate), which plays a key role in one-carbon metabolism, is essential for the biosynthesis of several compounds. Folic acid deficiency is probably the most common vitamin deficiency in the United States, particularly among pregnant women and alcoholics. [Note: Leafy, dark green vegetables are a good source of folic acid.

A. Function of folic acid Tetrahydrofolate (THF), the reduced, coenzyme form of folate, receives one-carbon fragments from donors such as serine, glycine, and histidine and transfers them to intermediates in the synthesis of amino acids, purines, and thymidine monophosphate (TMP), a pyrimidine nucleotide found in DNA.

B. Nutritional anemias Anemia is a condition in which the blood has a lower than normal concentration of hemoglobin, which results in a reduced ability to transport oxygen. Nutritional anemias (that is, those caused by inadequate intake of one or more essential nutrients) can be classified according to the size of the red blood cells (RBCs) or mean corpuscular volume (MCV) observed in the individual . Microcytic anemia (MCV below normal), caused by lack of iron, is the most common form of nutritional anemia. The second major category of nutritional anemia, macrocytic (MCV above normal), results from a deficiency in folic acid, or vitamin B12. [Note: These macrocytic anemias are commonly called megaloblastic because a deficiency of either vitamin (or both) causes accumulation of large, immature RBC precursors, known as megaloblasts, in the bone marrow and the blood.]

58. c) Folic acid and B_6

[Ref: Lippincott's illustrated reviews, 6th Edition]



Serine: This amino acid arises from 3-phosphoglycerate, an intermediate in glycolysis , which is first oxidized to 3-phosphopyruvate and then transaminated to 3-phosphoserine. Serine is formed by hydrolysis of the phosphate ester. Serine can also be formed from glycine through transfer of a hydroxymethyl group by serine hydroxymethyltransferase using N5,N10-methylene-THF as the one-carbon donor. [Note: Selenocysteine (Sec), the 21st genetically encoded amino acid, is synthesized from serine and selenium while serine is attached to transfer RNA. Sec is found in several proteins such as glutathione peroxidase]

59. a) Antioxidant

[Ref: Lippincott's illustrated reviews, 6th Edition]

VITAMIN E

The E vitamins consist of eight naturally occurring tocopherols, of which α-tocopherol is the most active. The primary function of vitamin E is as an antioxidant in prevention of the nonenzymic oxidation of cell components (for example, peroxidation of polyunsaturated FAs by molecular oxygen and free radicals).

A. Distribution and requirements of vitamin E Vegetable oils are rich sources of vitamin E, whereas liver and eggs contain moderate amounts. The RDA for α-tocopherol is 15 mg/day for adults.

The vitamin E requirement increases as the intake of polyunsaturated FA increases to limit FA peroxidation.

B. Deficiency of vitamin E Newborns have low reserves of vitamin E, but breast milk (and formulas) contain the vitamin. Very-low-birth-weight infants may be given supplements to prevent the hemolysis and retinopathy associated with deficiency of vitamin E. When observed in adults, deficiency is usually associated with defective lipid absorption or transport. [Note: Abetalipoproteinemia, caused by a defect in the formation of chylomicrons (and VLDL), results in vitamin E deficiency .

C. Clinical indications Vitamin E is not recommended for the prevention of chronic disease, such as coronary heart disease or cancer. Clinical trials using vitamin E supplementation have been uniformly disappointing. For example, subjects in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study trial who received high doses of vitamin E not only lacked cardiovascular benefit but also had an increased incidence of stroke.

D. Toxicity of vitamin E Vitamin E is the least toxic of the fat-soluble vitamins, and no toxicity has been observed at doses of 300 mg/day (UL = 1,000 mg/day).

Populations consuming diets high in fruits and vegetables show decreased incidence of some chronic diseases. However, clinical trials have failed to show a definitive benefit from supplements of vitamins A, C, or E; multivitamins with folic acid; or antioxidant combinations for the prevention of cancer or cardiovascular disease.

60. c) malabsorption syndrome

VITAMIN A

The retinoids, a family of molecules that are related to dietary retinol (vitamin A), are essential for vision, reproduction, growth, and maintenanceof epithelial tissues. They also play a role in immune function. Retinoic acid, derived from oxidation of retinol, mediates most of the actions of the retinoids, except for vision, which depends on retinal, the aldehyde derivative of retinol.

Liver, kidney, cream, butter, and egg yolk are good sources of preformed vitamin A. Yellow, orange, and dark green vegetables and fruits are good dietary sources of the carotenes, which serve as precursors of vitamin A.

Malabsorption causes deficiency of all Fat Soluble Vitamins.

61. c) Vitamin E

Lipid peroxidation in vivo: In the living cells, lipids undergo oxidation to produce peroxides and free radicals which can damage the tissue. The free radicals are believed to cause inflammatory diseases, ageing, cancer/ atherosclerosis etc. It is fortunate that the cells possess antioxidants such as vitamin E, urate and superoxide dismutase to prevent in vivo lipid peroxidation.

62. b) Retinal

Structure of vitamin A Vitamin A is often used as a collective term for several related biologically active molecules (Figure 28.18). The term retinoids includes both natural and synthetic forms of vitamin A that may or may not show vitamin A activity.

1. Retinol: A primary alcohol containing a β-ionone ring with an unsaturated side chain, retinol is found in animal tissues as a retinyl ester with long-chain FAs.

2. Retinal: This is the aldehyde derived from the oxidation of retinol. Retinal and retinol can readily be interconverted.

3. Retinoic acid: This is the acid derived from the oxidation of retinal. Retinoic acid cannot be reduced in the body, and, therefore, cannot give rise to either retinal or retinol.

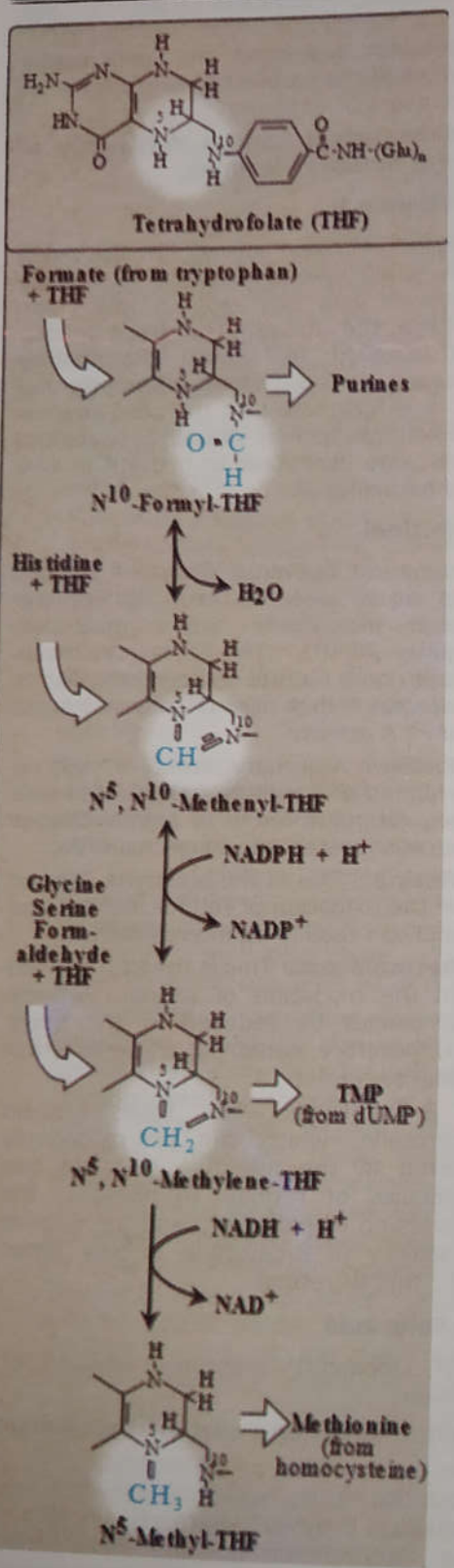
4. β-Carotene: Plant foods contain β-carotene, which can be oxidatively cleaved in the intestine to yield two molecules of retinal. In humans, the conversion is inefficient, and the vitamin A activity of β-carotene is only about 1/12 that of retinol.

63. a) Folic acid

[Ref: Lippincott's illustrated reviews, 6th Edition]

Folic acid and one-carbon metabolism

The active form of folic acid, THF, is produced from folate by dihydrofolate reductase in a two-step reaction requiring two nicotinamide adenine dinucleotide phosphates (NADPH). The one-carbon unit carried by THF is bound to nitrogen N5 or N10 or to both N5 and N10.



shows the structures of the various members of the THF family and their interconversions and indicates the sources of the onecarbon units and the synthetic reactions in which the specific members participate. [Note: Folate deficiency presents as a megaloblastic anemia due to decreased availability of the purines and of the thymidine monophosphate needed for DNA synthesis]

64. c) A coenzyme for one carbone transfer in nucleic acid mertbolism

Folate trap hypothesis

The effects of cobalamin deficiency are most pronounced in rapidly dividing cells, such as the erythropoietic tissue of bone marrow and the mucosal cells of the intestine. Such tissues need both the N5,N10-methylene and N10-formyl forms of THF for the synthesis of nucleotides required for DNA replication. However, in vitamin B12 deficiency, the utilization of the N5-methyl form of THF in the B12-dependent methylation of homocysteine to methionine is impaired. Because the methylated form cannot be converted directly to other forms of THF, folate is trapped in the N5-methyl form, which accumulates. The levels of the other forms decrease. Thus, cobalamin deficiency leads to a deficiency of the THF forms needed in purine and TMP synthesis, resulting in the symptoms of megaloblastic anemia.

65. d) All of the above

Clinical indications for thiamine

The oxidative decarboxylation of pyruvate and α-ketoglutarate, which plays a key role in energy metabolism of most cells, is particularly important in tissues of the CNS. In thiamine deficiency, the activity of these two dehydrogenase-catalyzed reactions is decreased, resulting in decreased production of ATP and, therefore, impaired cellular function. TPP is also required by branched-chain α-keto acid dehydrogenase of muscle. [Note: It is the decarboxylase of each

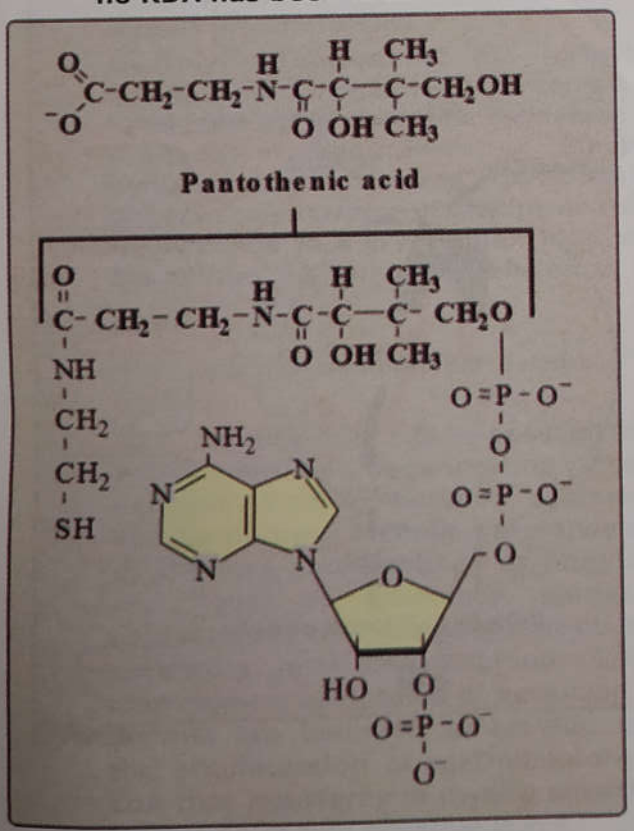
of these α-keto acid dehydrogenase multienzyme complexes that requires TPP.] Thiamine deficiency is diagnosed by an increase in erythrocyte transketolase activity observed on addition of TPP.]

66. e) Acetylation

[Ref: Lippincott's illustrated reviews, 6th Edition]

PANTOTHENIC ACID

Pantothenic acid is a component of CoA, which functions in the transfer of acyl groups . CoA contains a thiol group that carries acyl compounds as activated thiol esters. Examples of such structures are succinyl CoA, fatty acyl CoA, and acetyl CoA. Pantothenic acid is also a component of the acyl carrier protein domain of fatty acid synthas. Eggs, liver, and yeast are the most important sources of pantothenic acid, although the vitamin is widely distributed. Pantothenic acid deficiency is not well characterized in humans, and no RDA has been established.



67. d) Hyperostosis

[Ref: Lippincott's illustrated reviews, 6th Edition]

Toxicity of retinoids

Vitamin A: Excessive intake of vitamin A produces a toxic syndrome called hypervitaminosis A. Amounts exceeding 7.5 mg/day of retinol should be avoided. Early signs of chronic hypervitaminosis A are reflected in the skin, which becomes dry and pruritic (due to decreased keratin synthesis); the liver, which becomes enlarged and can become cirrhotic; and in the CNS, where a rise in intracranial pressure may mimic the symptoms of a brain tumor. Pregnant women particularly should not ingest excessive quantities of vitamin A because of its potential for teratogenesis (causing congenital malformations in the developing fetus). UL is 3,000 mg/day. [Note: Vitamin A promotes bone growth. In excess, however, it is associated with decreased bone mineral density and increased risk of fractures.]

68. d) Thiamine

Liver, kidney, cream, butter, and egg yolk are good sources of preformed vitamin A. Yellow, orange, and dark green vegetables and fruits are good dietary sources of the carotenes, which serve as precursors of vitamin A.

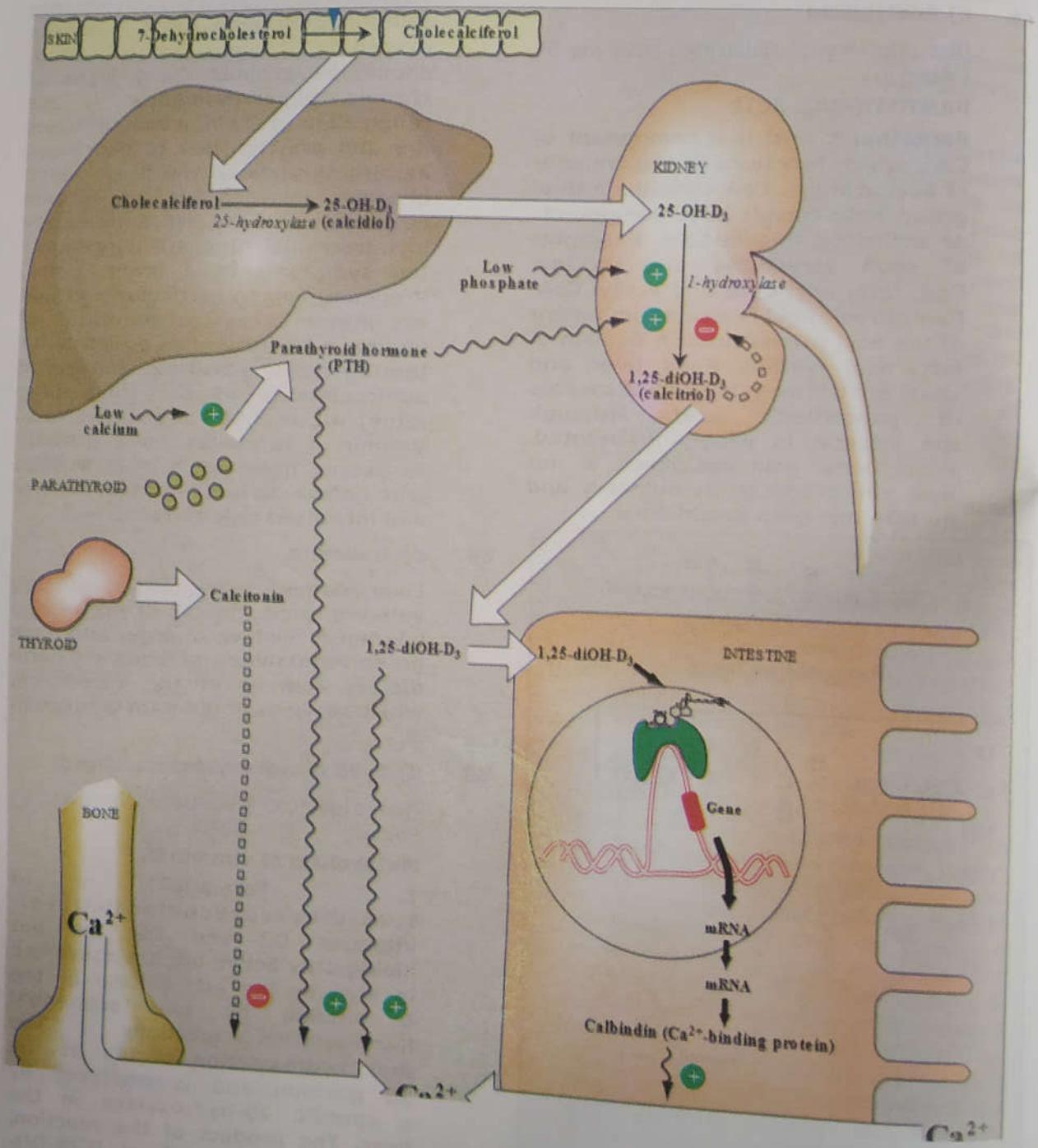
69. d) 1, 25 dihydroxycholecalciferol

[Ref: Lippincott's illustrated reviews, 6th Edition]

Metabolism of vitamin D

1. Formation of 1,25-dihydroxycholecalciferol: Vitamins D2 and D3 are not biologically active but are converted in vivo to the active form of the D vitamin by two sequential hydroxylation reactions . The first hydroxylation occurs at the 25 position and is catalyzed by a specific 25-hydroxylase in the liver. The product of the reaction, 25-hydroxycholecalciferol ([25-OH-

D3], calcidiol), is the predominant form of vitamin D in the plasma and the major storage form of the vitamin. 25-OH-D3 is further hydroxylated at the 1 position by 25-hydroxycholecalciferol 1-hydroxylase found primarily in the kidney, resulting in the formation of 1,25-diOH-D3 (calcitriol). [Note: This 1-hydroxylase, as well as the liver 25-hydroxylase, are cytochrome P450 (CYP) proteins .]



2. Regulation of 25 - hydroxycholecalciferol 1- hydroxylase: 1, 25-diOH- D3 is the most potent vitamin D metabolite. Its formation is tightly regulated by the level of plasma phosphate and calciumions. 25-Hydroxycholecalciferol 1- hydroxylase activity is increased directly by low plasma phosphate or indirectly by low plasma calcium, which triggers the secretion of parathyroid hormone (PTH) from the chief cells of the parathyroid gland. PTH upregulates the 1-hydroxylase. Thus, hypocalcemia caused by insufficient dietary calcium results in elevated levels of plasma 1,25-diOH-D3. [Note: 1,25-diOH-D3 inhibits synthesis of PTH, forming a negative feedback loop. It also inhibits activity of the 1-hydroxylase.]

70. c) Pyriodoxine

[Ref: Lippincott's illustrated reviews, 6th Edition]

Tryptophan is catabolised using Kynurenine Pathway:

Hydrolytic removal of the formyl group of N-formylkynurenine, catalyzed by kynurenine formylase, produces kynurenine. Since kynureninase requires pyridoxal phosphate, excretion of xanthurenate in response to a tryptophan load is diagnostic of vitamin B6 deficiency.

71. b) B_{12}

[Ref: Lippincott's illustrated reviews, 6th Edition]

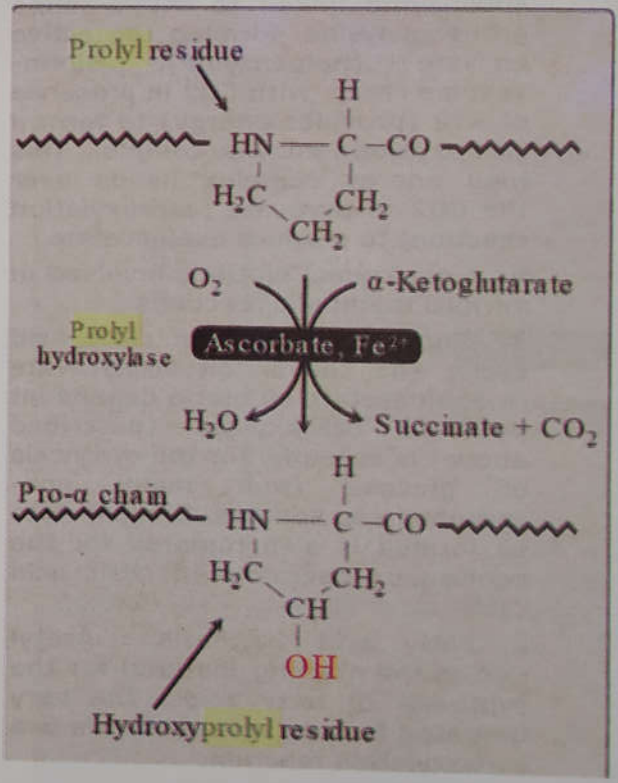
B12 deficiency is associated with neuronal degeneration and demyelination of nervous system. The symptoms include paresthesia (numbness and tingling) of fingers and toes. In advanced stages, confusion, loss of memory and even psychosis may be observed. The neurological symptoms of pernicious anemia are believed to be due to the accumulation of methylmalonyl CoA that interferes in myelin sheath formation in two possible ways.

1. The biosynthesis of fatty acids, required for myelin formation, is imparied. This is because, methylmalonyl CoA acts as a competitive inhibitor of malonyl CoA in fatty acid synthesis.

2. Methylmalonyl CoA can substitute malonyl CoA in fatty acid synthesis, resulting in a new type of branched chain fatty acids. These fatty acids will disrupt the normal membrane structure.The excretion of methylmalonic acid (elevated) in urine and estimation of serum B12 level are used to assess B12 deficiency.

72. a) Vitamin C mediated hydroxylation

[Ref: Lippincott's illustrated reviews, 6th Edition]



73. b) Carboxylation

[Ref: Satyanarayan 4th Edition]

Biotin (formerly known as anti-egg white injury factor, vitamin 87 or vitamin H) is a sulfur containing B-complex vitamin. It directly participates as a coenzyme in the carboxylation reactions.

Boas (I 927) observed that rats fed huge quantity of raw egg white developed dermatitis and nervous manifestations, besides retardation in growth. She however, found that feeding cooked egg did not produce any of these symptoms. It was later shown that the egg white injury in rats and chicks was due to the presence of an anti-vitamin in egg white. The egg-white injury factor was identified as a glycoprotein avidin and biotin was called as anti-egg white injury factor.

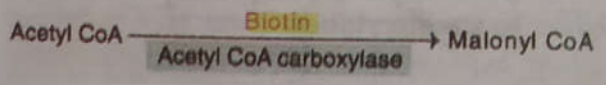
Biochemical functions:

Biotin serves as a carrier of COz in carboxylation reactions. The reaction cataiysed by pyruvate carboxylase, converting pyruvate to oxaloacetate has been investigated in detail. This enzyme has biotin bound to the apoenzyme linked to the e-amino group of lysine, forming the active enzyme (holoenzyme). Biotin-enzyme reacts with CO2 in presence of ATP (provides energy) to form a carboxybiotin-enzyme complex. This high energy complex hands over the CO2 to pyruvate (carboxylation reaction) to produce oxaloacetate

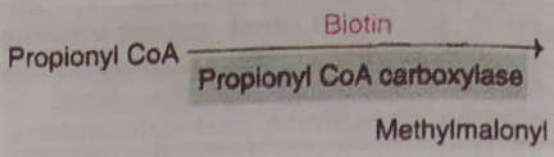
As a coenzyme, biotin is involved in various metabolic reactions.

1. Gluconeogenesis and citric acid cycle: The conversion of pyruvate to oxaloacetate by biotin dependent pyruvate carboxylase (described above) is essential for the synthesis of glucose from many non-carbohydrate sources. Oxaloacetate so formed is also required for the continuous operation of citric acid cycle.

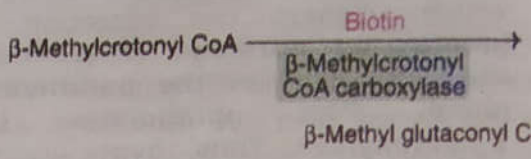
2. Fatty acid synthesis : Acetyl CoA is the starting material for the synthesis of fatty acids. The very first step in fatty acid synthesis is a carboxylation reaction.



3. Propionyl CoA is produced in the metabolism of certain amino acids (valine, isoleucine, threonine etc.) and degradation of odd chain fatty acids. Its further metabolism is dependent on biotin.



4. In the metabolism of leucine, the following reaction is dependent on biotin.



74. a) Vitamin C

Sparing action of other vitamins : Ascorbic acid is a strong antioxidant. It spares vitamin A, vitamin E, and some B-complex vitamins from oxidation.

75. b) Anaemia

Deficiency symptoms:

The symptoms of biotin deficiency include anemia, loss of appetite, nausea, dermatitis, glossitis etc. Biotin deficiency may also result in depression, hallucinations, muscle pain and dermatitis,

Biotin deficiency is uncomrnon, since it is well distributed in foods and also supplied by the intestinal bacteria. The deficiency may however, be associated with the following two causes.

1. Destruction of intestinal flora due to prolonged use of drugs such as sulfonamides.

2. High consumption of raw eggs. The raw egg white contains a glycoprotein avidin, which tightly binds with biotin and blocks its absorption from the intestine. An intake of about 20 raw eggs per day is needed to produce biotin deficiency symptoms in humans. Consumption of an occasional raw egg will not result in deficiency.

Antagonists

Desthiobiotin, biotin sulphonic acid are biotin antagonists.

76. b) B2

77. b) Vitamin B_2

The two biologically active forms of B2 are flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD), formed by the transfer of an adenosine monophosphate moiety from ATP to FMN. FMN and FAD are each capable of reversibly accepting two hydrogen atoms, forming FMNH2 or FADH2. FMN and FAD are bound tightly, sometimes covalently, to flavoenzymes (for example, NADH dehydrogenase [FMN] and succinate dehydrogenase [FAD]) that catalyze the oxidation or reduction of a substrate. Riboflavin deficiency is not associated with a major human disease, although it frequently accompanies other vitamin deficiencies. Deficiency symptoms include dermatitis, cheilosis (fissuring at the corners of the mouth), and glossitis (the tongue appearing smooth and dark).

78. b) Vitamin C

All water soluble Vitamins are excreted in the Urine.

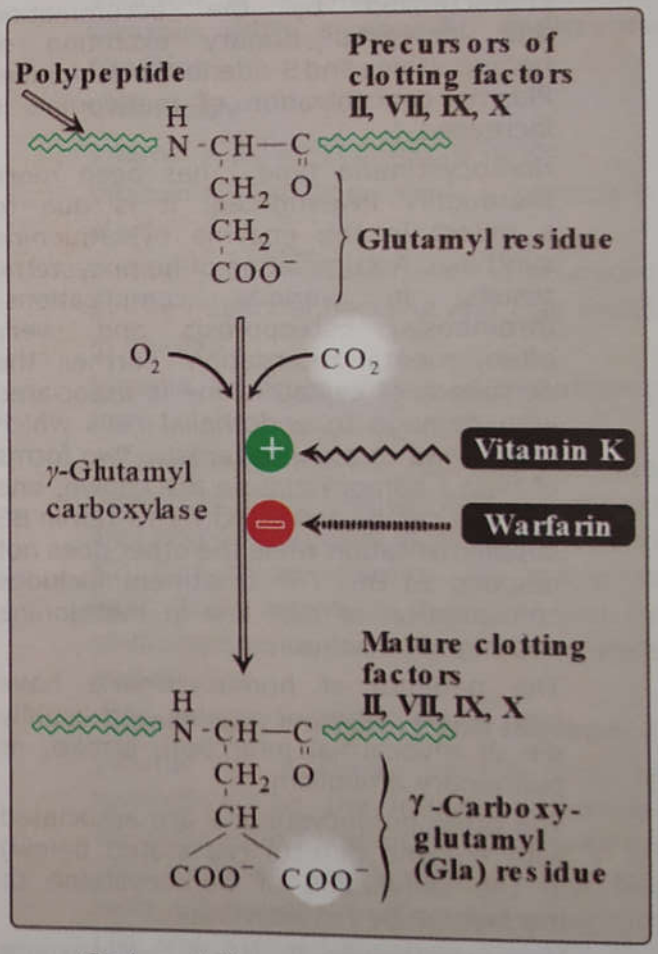
79. a) Avidin

Biotin is a coenzyme in carboxylation reactions, in which it serves as a carrier of activated carbon dioxide .Biotin is covalently bound to the ε-amino group of lysine residues in biotin-dependent enzymes. Biotin deficiency does not occur naturally because the vitamin is widely distributed in food. Also, a large percentage of the biotin requirement in humans is supplied by intestinal bacteria. However, the addition of raw egg white to the diet as a source of protein induces symptoms of biotin deficiency, namely, dermatitis, glossitis, loss of appetite, and nausea. Raw egg white contains a glycoprotein, avidin, which tightly binds biotin and prevents its absorption from the intestine. With a normal diet, however, it has been estimated that 20 eggs/day would be required to induce a deficiency syndrome. Thus, inclusion of an occasional raw egg in the diet does not lead to biotin deficiency, although eating raw eggs is generally not recommended due to the possibility of salmonella infection.

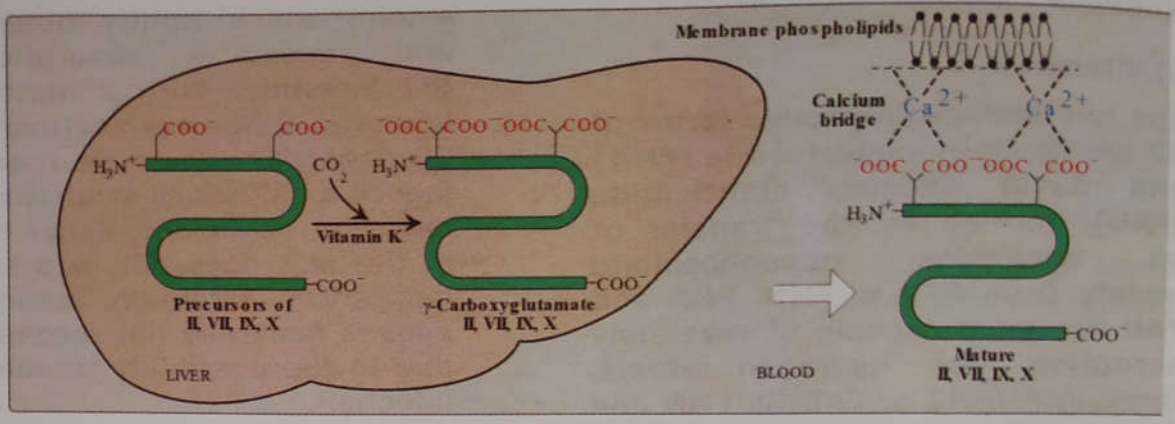
Anti-vitamins : Avidin of raw egg is a good example of anti-vitamin of biotin

80. d) Carboxxylation

[Ref: Lippincott's illustrated reviews, 6th Edition]



Carboxylation of glutamate to form γ-carboxyglutamate.



Role of vitamin K in blood coagulation.

81. d) B6

[Ref: Satyanarayan 4th Edition]

Homocystinurias : Homocystinurias are a group of metabolic disorders characterized by the accumulation and increased urinary excretion of homocysteine and S-adenosylmethionine. Plasma concentration of methionine is increased.

Homocystinuria type I has been more thoroughly investigated. It is due to a defect in the enzyme cystathionine synthase. Accumulation of homocystetne results in various complications-thrombosis, osteoporosis and, very often, mental retardation. Further, the deficiency of cystathionine is associated with damage to endothelial cells which might lead to atherosclerosis. Two forms of type I homocystinuria are known, one of them can be corrected with vitamin B6 supplementation while the other does not respond to B6. The treatment includes consumption of diet low in methionine and high in cystine.

The patients of homocystinuria have high levels of homocysteine, and usually die of myocardial infarction, stroke, or pulmonary embolism.

The other homocystinuria are associated with enzyme defects (as stated below) in the conversion of homocysteine to methionine by remethylation.

Homocystinuria II: N5-N1O-Methylene THF reductase.

Homocystinuria III: N5-N1O - Methyl THF homocysteine methyl transferase. This is mostly due to impairment in the synthesis of methylcobalamin.

Homocystinuria IV : Ns-Methyl THF homocysteine methyl transferase. This is primarily due to a defect in the intestinal absorption of vitamin B12.

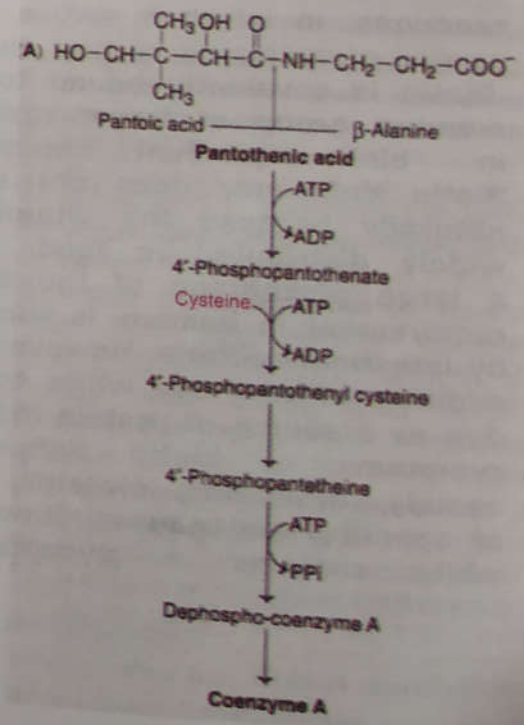
82. c) Pyridoxal phosphate

[Ref: Satyanarayan 4th Edition]

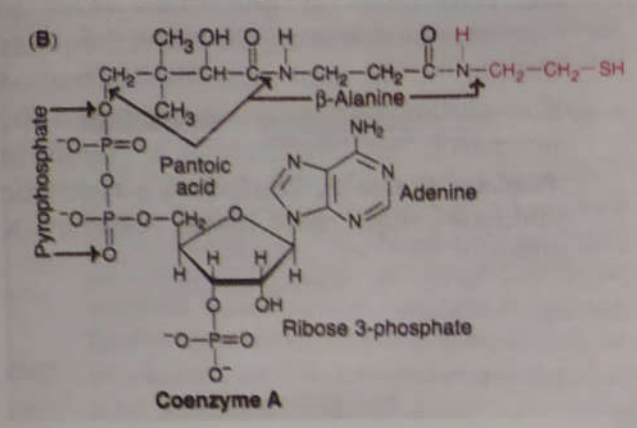
Pantothenic acid formerly known as chick anti-dermatitis factor (or filtrate factor) is widely distributed in nature. It's metabolic role as coenzyme A is also widespread.

Chemistry and synthesis of coenzyme A

Pantothenic acid consists of two components, pantoic acid and p-alanine, held together by a peptide linkage. Synthesis of coenzyme A from pantothenate occurs in a series of reactions:



Pantothenate is first phosphorylated to which cysteine is added.



Decarboxylation, followed by addition of AMP moiety and a phosphate (each from ATP) results in coenzyme A. The structure of coenzyme A consists of pantothenic acid joined to p-mercaptoethanolamine (thioethanolamine) at one end. On the other side, pantothenic acid is held by a phosphate bridge to adenylic acid. The adenylic acid is made up of adenine, and a phosphate linked to carbon-3 of ribose.

83. d) Polyneuritis

[Ref: Satyanarayan 4th Edition]

Vitamin A, administered as retinol or retinyl esters, is used to treat patients who are deficient in the vitamin. Night blindness is one of the earliest signs of vitamin A deficiency. The visual threshold is increased, making it difficult to see in dim light. Prolonged deficiency leads to an irreversible loss in the number of visual cells. Severe vitamin A deficiency leads to xerophthalmia, a pathologic dryness of the conjunctiva and cornea, caused, in part, by increased keratin synthesis. If untreated, xerophthalmia results in corneal ulceration and, ultimately, in blindness because of the formation of opaque scar tissue. The condition is most commonly seen in children in developing tropical countries. Over 500,000 children worldwide are blinded each year by xerophthalmia caused by insufficient vitamin A in the diet.

Acne and psoriasis: Dermatologic problems such as acne and psoriasis are effectively treated with retinoic acid or its derivatives . Mild cases of acne, Darier disease (keratosis follicularis), and skin aging are treated with topical application of tretinoin (all-trans retinoic acid), as well as benzoyl peroxide and antibiotics. [Note: Tretinoin is too toxic for systemic administration and is confined to topical application.] In patients with severe cystic acne unresponsive to conventional therapies, the drug of choice is isotretinoin (13-cis retinoic acid) administered orally. Retinoic acid is also used in the treatment of acute promyelocytic leukemia.

84. d) Deficiency leads to shortened PT

[Ref: Satyanarayan 4th Edition]

Vitamin K is the only fat soluble vitamin with a specific coenzyme function.

Chemistry

Vitamin K exists in different forms-

Vitamin K1 (phylloquinone) is present in plants.

Vitamin K2 (menaquinone) is produced by the intestinal bacteria and also found in animals.

Vitamin K3 (menadione) is a synthetic form.

All the three vitamins (K1 , K2, K3) are naphthoquinone derivatives. Isoprenoid side chain is present in vitamins Kt and K2. The three vitamins are stable to heat. Their activity is, however, lost by oxidizing agents, irradiation, strong acids and alkalies.

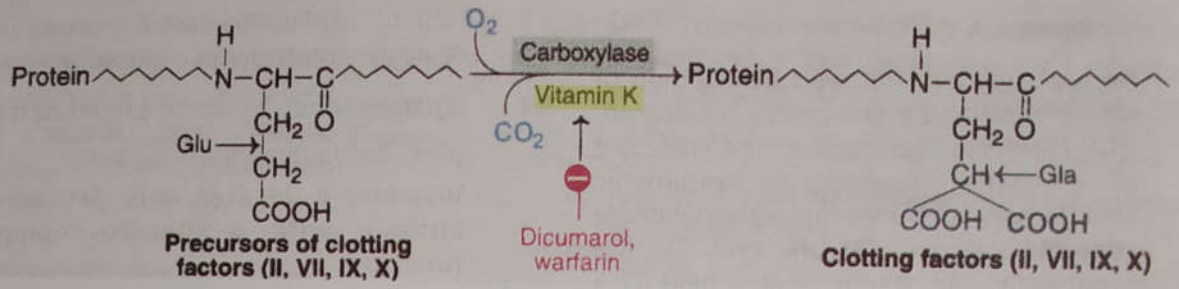
Absorption, transport and storage

Vitamin K is taken in the diet or synthesized by the intestinal bacteria. Its absorption takes place along with fat (chylomicrons) and is dependent on bile salts. Vitamin K is transported along with LDL and is stored mainly in liver and, to a lesser extent, in other tissues.

Biochemical functions

The functions of vitamin K are concerned with blood clotting process. It brings

about the posttranslational (after protein biosynthesis in the cell) modification of certain blood clotting factors. The clotting factors II (prothrombin), VII, IX and X are synthesized as inactive precursors (zymogens) in the liver. Vitamin K acts as a coenzyme for the carboxylation of glutamic acid residues present in the proteins and this reaction is catalysed by a carboxylase (microsomal). It involves the conversion of glutamate (Clu) to y-carboxyglutamate (Gla) and requires vitamin K, 02 and CO2.The formation of y-carboxyglutamate is inhibited by dicumarol, an anticoagulant found in spoilt sweet clover. Warfarin is a synthetic analogue that can inhibit vitamin K action.

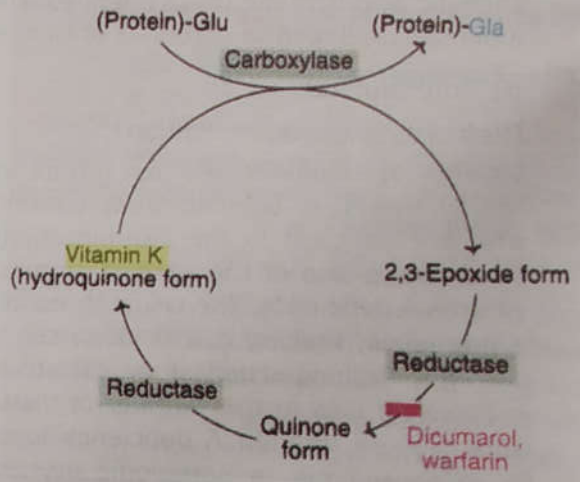


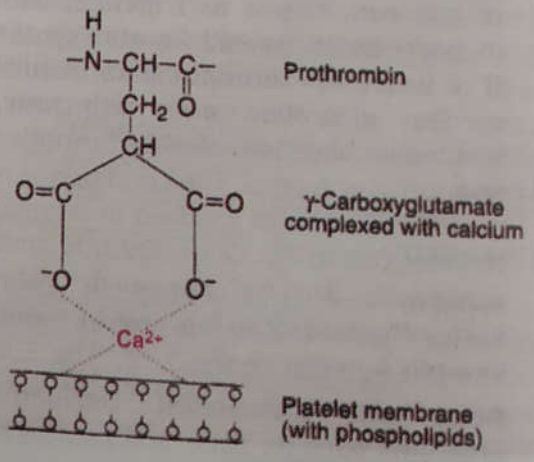
Vitamin K is also required for the carboxylation of glutamic acid residues of osteocalcin, a calcium binding protein present in the bone.

The mechanism of carboxylation is not fully understood. It is known that a 2,3-epoxide derivative of vitamin K is formed as. An intermediate during the course of the reaction. Dicumarol inhibits the enzyme (reductase) that converts epoxide to active vitamin K.

Role of Gla in clotting :

The Gamma carboxyglutamic acid (Gla) residues of clotting factors are negatively charged (COO-) and they combine with positively charged calcium ions (Ca2+) to form a complex. The mechanism of action has been studied for prothrombin. The prothrombin -Ca complex binds to the phospholipids on the membrane surface of the platelets. This leads to the increased conversion of prothrombin to thrombin.





Dietary sources

Cabbage, cauliflower, tomatoes, alfa alfa, spinach and other green vegetables are good sources. It is also present in egg yolk, meat, liver, cheese and dairy products.

Deficiency symptoms:

The deficiency of vitamin K is uncommon, since it is present in the diet in sufficient quantity and/or is adequately synthesized by the intestinal bacteria. However, vitamin K deficiency may occur due to its faulty absorption (lack of bile salts), loss of vitamin into feces (diarrheal diseases) and administration of antibiotics (killing of intestinal flora).

Deficiency of vitamin K leads to the lack of active prothrombin in the circulation. The result is that blood coagulation is adversely affected. The individual bleeds profusely even for minor injuries. The blood clotting time is increased.

Hypervitaminosis K

Administration of large doses of vitamin K produces hemolytic anaemia and jaundice, particularly in infants. The toxic effect is due to increased breakdown of RBC.

Antagonists of vitamin K

The compounds-namely heparin, bishydroxycoumarin-act as anticoagulants and are antagonists to vitamin K. The salicylates and dicumarol are also antagonists to vitamin K.

Dicumarol is structurally related to vitamin K acts as a competitive inhibitor in the synthesis of solution.

85. b) D

Vitamin D is a fat soluble vitamin. It resembles sterols in structure and functions like a hormone. Vitamin D is absorbed in the small intestine for which bile is essential. Through lymph, vitamin D enters the circulation bound to plasma a2-globulin and is distributed throughout the body. Liver and other tissues store small amounts of vitamin D.

86. b) >1% prevalence of night-blindness is the criteria for determining the xerophthalmia problem in the population at risk (6m-6yr) d) Chronic vitamin A intoxication causes papilledema

a. 1600 U retinal is used for treatment of xerophthalmia-

WHO is according high priority to prevention in communities where xerophthalmia occurs, giving single prophylactic oral doses of 60mg retinyl palmitate (providing 200 000U retinol) to pre-school children. This also reduces mortality from gastroenteritis and respiratory infections

b. >1% prevalence of night-blindness is the criteria for determining the xerophthalmia problem in the population at risk (6m-6yr)

(Park 24th/654): Prevalence criteria for determining the xerophthalmia problem

Criteria	Prevalence in the population at risk (6m-6yr)
Night blindness	More than 1%
Bitot's spots	More than 0.5%
Corneal xerosis/corneal ulceration/Keratomalacia	More than 0.01%
Corneal ulcer	More than 0.05%
Serum retinol (<10 mcg/dl)	More than 5%

c. Retinal is not present in milk –

Vit. A is found in animal as preformed Vit.A (retinol) and in plant as provitamins (carotenes). Animal foods rich in retinol are liver, eggs, butter, cheese, whole milk, fish and meat. Fish liver oils are the richest natural sources of retinol"- Park 24th/653

d. Chronic vitamin A intoxication causes papilledema-

Toxicity of Vit. A: Nausea, vomiting, anorexia and sleep disorders followed by skin desquamation and then an enlarged liver and papillar edema"-Park 24th/654

Heme Metabolism – Questions

Q1. Coproporphyrin – III is

a. Abnormal haemoglobin precursor
b. Normal HB break down product
c. Excreted in lead poisoning
d. Normally excreted in urine
e. Excreted in hepatic porphyria

As can be seen from the table it is excreted in hepatic porphyria.

Q2. Storage from of iron in body is:

a. Ferritin b. Transferrin
c. Hemosiderin d. None of the above

Q3. All are true except

a. Porphyrinogens are coloured
b. Porphyrins emit flurorescence by UV light
c. Pyrrole rings of porphyrins are joint by metheny bridge
d. Pyrrole rings of porphyringogens are joint by methylene bridge

Q4. Rate limiting enzyme in heme synthesis

a. Ala synthase
b. HMG coa reductase
c. ALA dehydratase
d. Uroporphyrinogen 1 synthase

Q5. Iron in the hemoglobin is held by

a. Polar bonds
b. Non polar bonds
c. Co-ordinate bonds
d. Covalent bonds

Q6. HbS has defect in amino acid position

a. 4 b. 6
c. 11 d. 12

Q7. Hemoproteins are

a. Cytochrome C b. Cytochrome 450
c. Myoglobin d. Hemoglobin
e. Catalase

Q8. Carbon monoxide combines with

a. Heme part of hemoglobin
b. Glubin part of bhemoglobin
c. Myglobin
d. Plasma

Q9. Hemoprosthetic group is found in

a. Myoglobin
b. Cytochrome oxidase
c. Xanthine oxidase
d. Tyrosine

Q10. Pigment providing clour to stool is

a. Stercobilinogen b. Urobilinogen
c. Mevobilirubin d. Bilirubin

Q11. The conjugation of bilirubin to glucuronic acid in the liver –

a. Convetes a hydrophilic compound to a hydrophobic one
b. Converts a hydrophobic compound to a hydrophilic one
c. Enables the bilirubin molecule to cross the cell membrane
d. Is increased during neonatal jaundice

Q12. Which of the following are metalloporphyrin:

a. Hemoglobin b. Catalase
c. Bilibrubin d. Cytochrome
e. Pyrolase

Q13. Iron is complexd in hemoglobin to-

a. Leucine b. Histidine
c. Isoleucine d. Valine

Q14. Myoglobin –

a. Contains four hemes per molecule
b. Shows the Bohr Effect
c. Has an O2 dissociation curve that is unaffected by wide range of pH
d. None of the above.

1. c, e	2. a	3. a	4. a	5. a	6. b	7. all	8. a, c	9. a, b	10. a
11. b	12. a, b, d, e	13. b	14. c						

Q15. False Statement about haemoglobin structure –

a. Hb has 2 polypeptide
b. Iron is present in ferrous state
c. Hb structurally similar to myoglobin
d. Ferrous ions are in porphyrin rings

Q16. Which of the following conditions promote the dissociation of 02 from hemoglobin?

a. Decrease in pH
b. Increase in 2, 3 diphosphoglycerate concentration
c. Increase in $C0_2$ concentration
d. Increase in the partial pressure of 0_2

Q17. Embryonic hemoglobin is

a. alpha, $beta_2$ b.$alpha_2$ $epsilon_2$
c. $alpha_2$ gamma d. $alpha_1$ $epsilon_2$

Q18. Bohr effect is

a. Effect on Zn on carbonic anhydrase activity
b. Effect of PC02 on oxyhemoglobin dissociation
c. HC03 leaving the RBC in exchange of CI
d. H leaving RBC for each C02 that inters

Q19. Which of the following statement characterize both Hemoglobin and Myoglobin?

a. Non-helical
b. Subunits are held together by hydrogen bonds
c. Binds with 2 Heme
d. Heme at hydrophobic pockets
e. Bind with 1 molecule of O2

Q20. Which of the following is correct about breakdown of hemoglobin(Hb)

a. Hb -> Heme ->bilirubin ->urobilinogen
b. Heme->Hb -> biliverdin -> urobilinogen
c. Hb -> Heme ->biliverdin ->bilirubin ->urobilinogen
d. Hb->Heme ->bilirubin ->urobilingen ->biliverdin

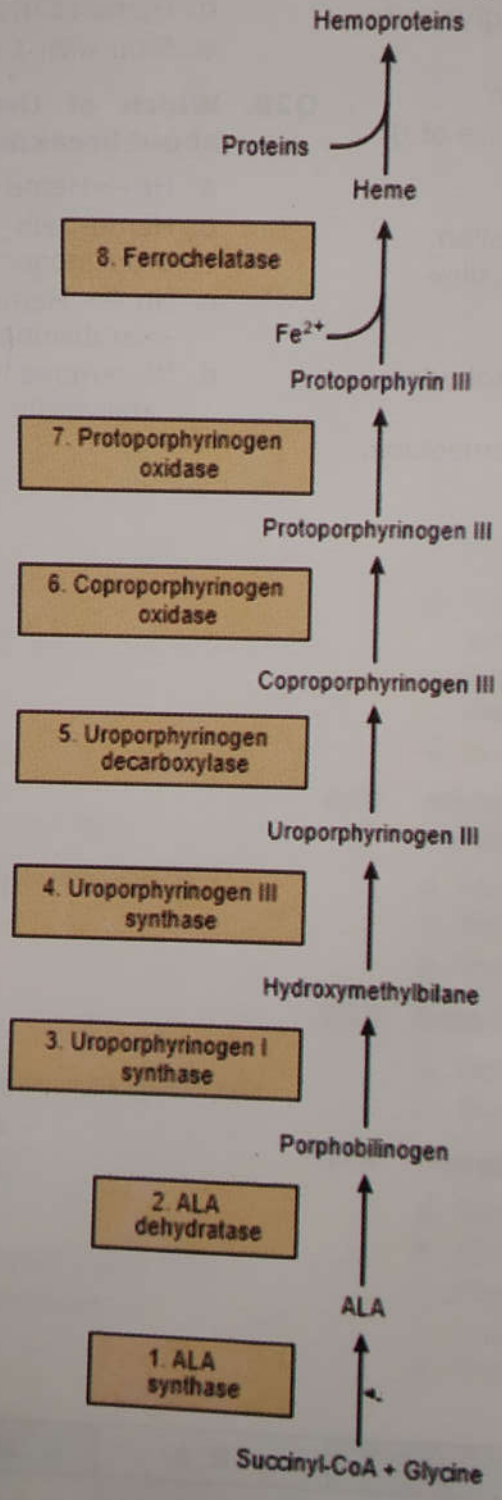
15. a, c	16. a, b, c	17. b	18. b	19. d	20. c

Heme Metabolism – Explanations

1. c) Excreted in lead poisoning
e) Excreted in hepatic porphyria

[Ref: Harper's Illustrated biochemistry, 28th Edition]

a. Abnormal haemoglobin precursor-normal hemoglobin prescorsor.



b. Normal HB break down product-it is formed during heme synthesis. And is not a break down product. Catabolism of heme produces bilirubin.

c. Excreted in lead poisoning-

High levels of lead can affect heme metabolism by combining with SH groups in enzymes such as ferrochelatase and ALA dehydratase. This affects porphyrin metabolism. Elevated levels of protoporphyrin are found in red blood cells, and elevated levels of ALA and of coproporphyrin are found in urine.

d. Normally excreted in urine –

normally not seen in urine.

e. Excreted in hepatic porphyria-

Enzyme Involved[2]	Type, Class and OM/M Number	Major signs and symptoms	Results of Laboratory Tests
1. ALA synthase (lerythroid form)	X-Linked sideroblastic anemia (erythropdietic) (OM/M 301300)	Anemia	Red cell count and hemolobin decreased
2. ALA dehydrates	ALA dehydrates deficiency (hepatic) (OM/M 125270)	Abdominal pain, neuropsychiatric symptoms	Urinary ALA and coproporphyin III increased
3. Uroporphyinogen I synthase	Congenital erythropoietic (erythropietic) (OM/M 176000)	Abdominal pain, neuropsychiatric symptoms	Urinary ALA and PBG increased
4. Uroporphyrrinogen III	Congenital erythropoietic (erythropoietic) (OM/M 263000)	Photosensitivity	Urinary fecal and red cell uroporphyin increased
5. Uroporphyinogen decarboxylase	Porphyria cutanea tarda (hepatic) (OM/M 176000)	Photosensitivity	Urinary uroporphyin I increased
6. Coproporphyrinogen oxidase	Herediary coproporphyria (hepatic) (OM/M 121300)	Photosensitivity, abdominal pain, neuropsychiatric symptoms	Urinary ALA, PBG and corproporphyin III and fecal coproporphyrin III increased
7. Protoporphyinogen	Variegate porphyria (hepatic) (OM/M 176200)	Photosensitivity, abdominal pain, neuropsychiatric symptoms	Urinary ALA, PBG and coproporphyrin III and fecal protoporphyrin IX increased
8. Ferrochelatase	Protoporphyria (erythropoietic) (OM/M 177000)	Photosensitivity	Fecal and red cell protoporphyrin IX increased

As can be seen from the table it is excreted in hepatic porphyria.

2. a) Ferritin

[Ref: Harper's Illustrated biochemistry, 28th Edition]

a. Ferritin-

Ferritin Stores Iron in Cells Ferritin is another protein that is important in the metabolism of iron. Under normal conditions, it stores iron that can be called upon for use as conditions require. In conditions of excess iron (eg, hemochromatosis), body stores of iron are greatly increased and much more ferritin is present in the tissues, such as the liver and spleen. Ferritin contains approximately 23% iron, and apoferritin (the protein moiety free of iron) has a molecular mass of approximately 440 kDa. Ferritin is composed of 24 subunits of 18.5 kDa, which surround in a micellar form some 3000 to 4500 ferric atoms. Normally, there is a little ferritin in human plasma. However, in patients with excess iron, the amount of ferritin in plasma is markedly elevated. The amount of ferritin in plasma can be conveniently measured by a sensitive and specific radioimmunoassay and serves as an index of body iron stores.

b. Transferrin-

Transferrin (Tf) is a plasma protein that plays a central role in transporting iron around the body to sites where it is needed.

Transferrin (Tf) is a β1-globulin with a molecular mass of approximately 76 kDa. It is a glycoprotein and is synthesized in the liver. About 20 polymorphic forms of transferrin have been found. It plays a central role in the body's metabolism of iron because it transports iron (2 mol of Fe3+ per mole of Tf) in the circulation to sites where iron is required, eg, from the gut to the bone marrow and other organs. Approximately 200 billion red blood cells (about 20 mL) are catabolized per day, releasing about 25 mg of iron into the body—most of which will be transported by transferrin.

c. Hemosiderin-

Hemosiderin is a somewhat ill-defined molecule; it appears to be a partly degraded form of ferritin but still containing iron. It can be detected by histologic stains (eg, Prussian blue) for iron, and its presence is determined histologically when excessive storage of iron occurs.

d. None of the above

3. a) Porphyrinogens are coloured

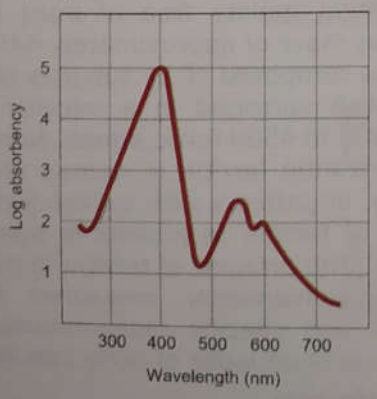
[Ref: Harper's Illustrated biochemistry, 28th Edition]

a. Porphyrinogens are coloured –

The porphyrinogens are colorless, containing six extra hydrogen atoms as compared with the corresponding colored porphyrins. These reduced porphyrins (the porphyrinogens) and not the corresponding porphyrins are the actual intermediates in the biosynthesis of protoporphyrin and of heme.

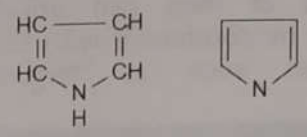
b. Porphyrins emit flurorescence by UV light-

Porphyrins are colored & fluoresce

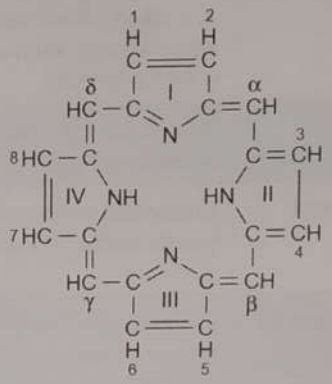


Absorption spectrum of hematoporphyrin (0.01% solution in 5% HCl).

c. Pyrrole rings of porphyrins are joint by metheny bridge-



Pyrrole



Porphyrin
($C_{20}H_{14}N_4$)

The porphyrin molecule. Rings are labeled I, II, III, and IV. Substituent positions on the rings are labeled 1, 2, 3, 4, 5, 6, 7, and 8. The methyne bridges (=HC—) are labeled α, β, γ, and δ. The numbering system used is that of Hans Fischer.

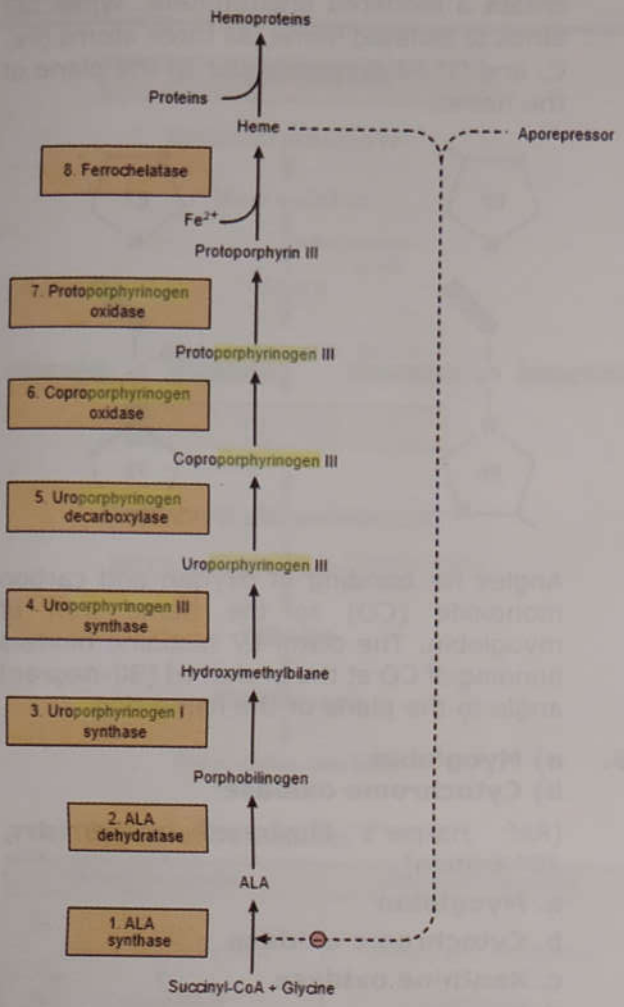
d. Pyrrole rings of porphyringogens are joint by methylene bridge

4. a) Ala synthase

[Ref: Harper's Illustrated biochemistry, 28th Edition]

a. Ala synthase-

ALA Synthase Is the Key Regulatory Enzyme in Hepatic Biosynthesis of Heme ALA synthase occurs in both hepatic (ALAS1) and erythroid (ALAS2) forms. The rate-limiting reaction in the synthesis of heme in liver is that catalyzed by ALAS1 ,a regulatory enzyme. It appears that heme, probably acting through an aporepressor molecule, acts as a negative regulator of the synthesis of ALAS1. This repression-derepression mechanism is depicted:



b. HMG coa reductase

c. ALA dehydratase

d. Uroporphyrinogen 1 synthase

5. a) Polar bonds

a. Polar bonds

b. Non polar bonds

c. Co-ordinate bonds

d. Covalent bonds

Structure of heme

Heme is a complex of protoporphyrin IX and ferrous iron (Fe2+) .The iron is held in the center of the heme molecule by bonds to the four nitrogens of the porphyrin ring. The heme Fe2+ can form two additional bonds, one on each side of the planar porphyrin ring. In myoglobin and hemoglobin, one of these positions is coordinated to the side chain of a histidine residue of the globin molecule, whereas the other position is available to bind oxygen .

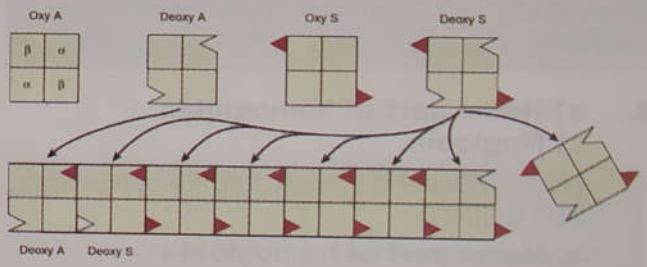
6. b) 6

[Ref: Harper's Illustrated biochemistry, 28th Edition]

a. 4

b. 6

Hemoglobin S In HbS, the nonpolar amino acid valine has replaced the polar surface residue Glu6 of the β subunit, generating a hydrophobic "sticky patch" on the surface of the β subunit of both oxyHbS and deoxyHbS. Both HbA and HbS contain a complementary sticky patch on their surfaces that is exposed only in the deoxygenated T state. Thus, at low Po2, deoxyHbS can polymerize to form long, insoluble fibers. Binding of deoxyHbA terminates fiber polymerization, since HbA lacks the second sticky patch necessary to bind another Hb molecule .



Representation of the sticky patch (Δ) on hemoglobin S and its "receptor" (Δ) on deoxyhemoglobin A and deoxyhemoglobin S. The complementary surfaces allow deoxyhemoglobin S to polymerize into a fibrous structure, but the presence of deoxyhemoglobin A will terminate the polymerization by failing to provide sticky patches.

These twisted helical fibers distort the erythrocyte into a characteristic sickle shape, rendering it vulnerable to lysis in the interstices of the splenic sinusoids. They also cause multiple secondary clinical effects. A low Po2 such as that at high altitudes exacerbates the tendency to polymerize. Emerging treatments for sickle cell disease include inducing HbF expression to inhibit the polymerization of HbS, stem cell transplantation, and, in the future, gene therapy.

c. 11

d.12

7. All

[Ref: Harper's Illustrated biochemistry, 28th Edition]

a. Cytochrome C

b. Cytochrome 450

c. Myoglobin

d. Hemoglobin

e. Catalase

Examples of Some Important Human and Animal Hemoproteins:

Protein	Function
Hemoglobin	Transport of oxygen in blood
Myoglobin	Storage of oxygen in muscle
Cytochrome c	Involvement in electron transport chain
Cytochrome P450	Hydroxylation of xenobiotics
Catalase	Degradation of hydrogen peroxide
Tryptophan pyrrolase	Oxidation of tryptophan

8. a) Heme part of hemoglobin
c) Myglobin

[Ref: Harper's Illustrated biochemistry, 28th Edition]

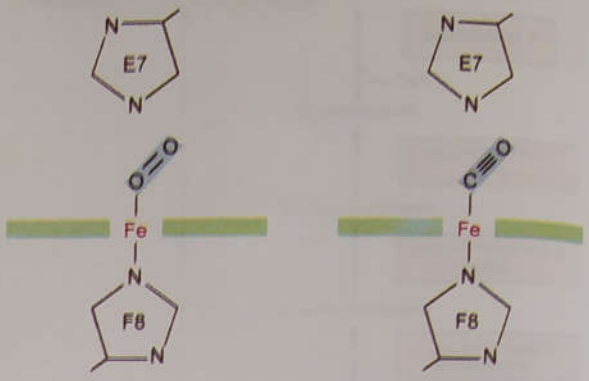
a. Heme part of hemoglobin

b. Glubin part of bhemoglobin

c. Myglobin

d. Plasma

Apomyoglobin Provides a Hindered Environment for Heme Iron When O2 binds to myoglobin, the bond between the first oxygen atom and the Fe2+ is perpendicular to the plane of the heme ring. The bond linking the first and second oxygen atoms lies at an angle of 121 degrees to the plane of the heme, orienting the second oxygen away from the distal histidine. Isolated heme binds carbon monoxide (CO) 25,000 times more strongly than oxygen. Since CO is present in small quantities in the atmosphere and arises in cells from the catabolism of heme, why is it that CO does not completely displace O2 from heme iron? The accepted explanation is thatthe apoproteins of myoglobin and hemoglobin create a hindered environment. When CO binds to isolated heme, all three atoms (Fe, C, and O) lie perpendicular to the plane of the heme.



Angles for bonding of oxygen and carbon monoxide (CO) to the heme iron of myoglobin. The distal E7 histidine hinders bonding of CO at the preferred (90-degree) angle to the plane of the heme ring.

9. a) Myoglobin
b) Cytochrome oxidase

[Ref: Harper's Illustrated biochemistry, 28th Edition]

a. Myoglobin

b. Cytochrome oxidase

c. Xanthine oxidase

d. Tyrosine

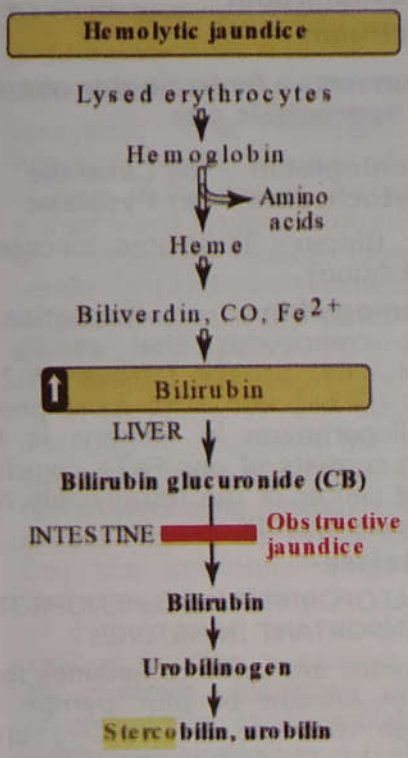
Examples of Some Important Human and Animal Hemoproteins:

Protein	Function
Hemoglobin	Transport of oxygen in blood
Myoglobin	Storage of oxygen in muscle
Cytochrome c	Involvement in electron transport chain
Cytochrome P450	Hydroxylation of xenobiotics
Catalase	Degradation of hydrogen peroxide
Tryptophan pyrrolase	Oxidation of tryptophan

10. a) Stercobilinogen

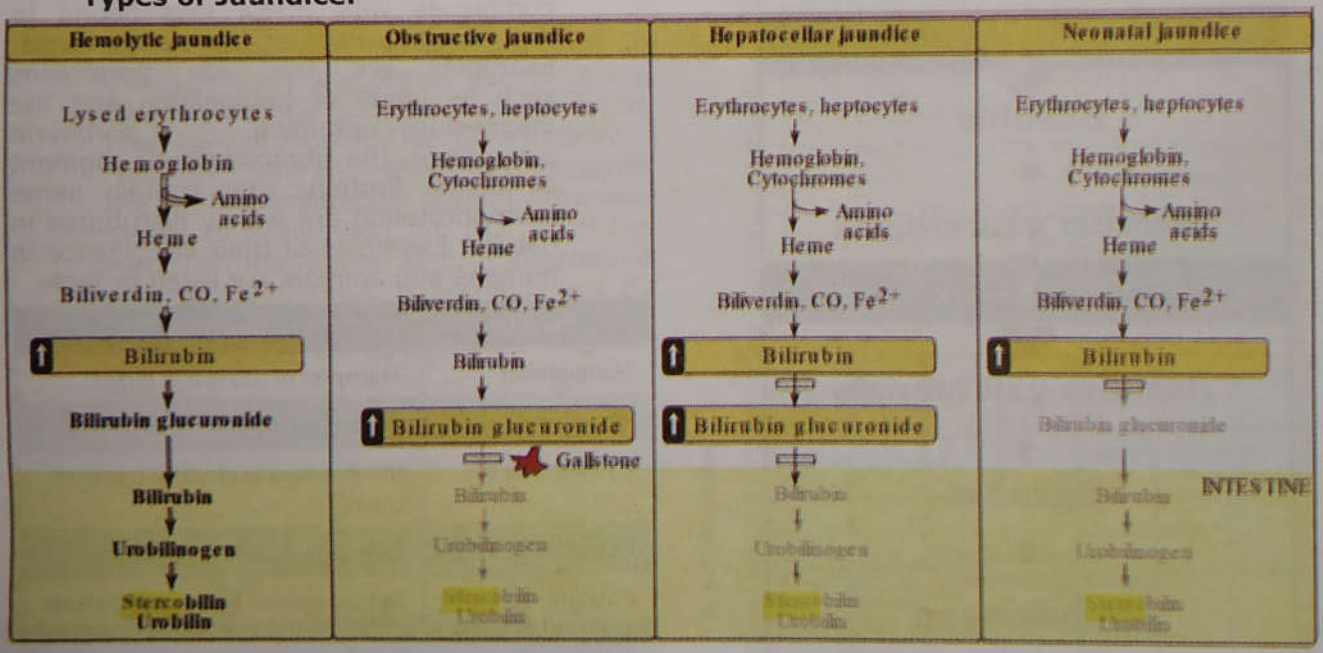
[Ref: Lippincott's illustrated reviews, 6th Edition]

a. Stercobilinogen –

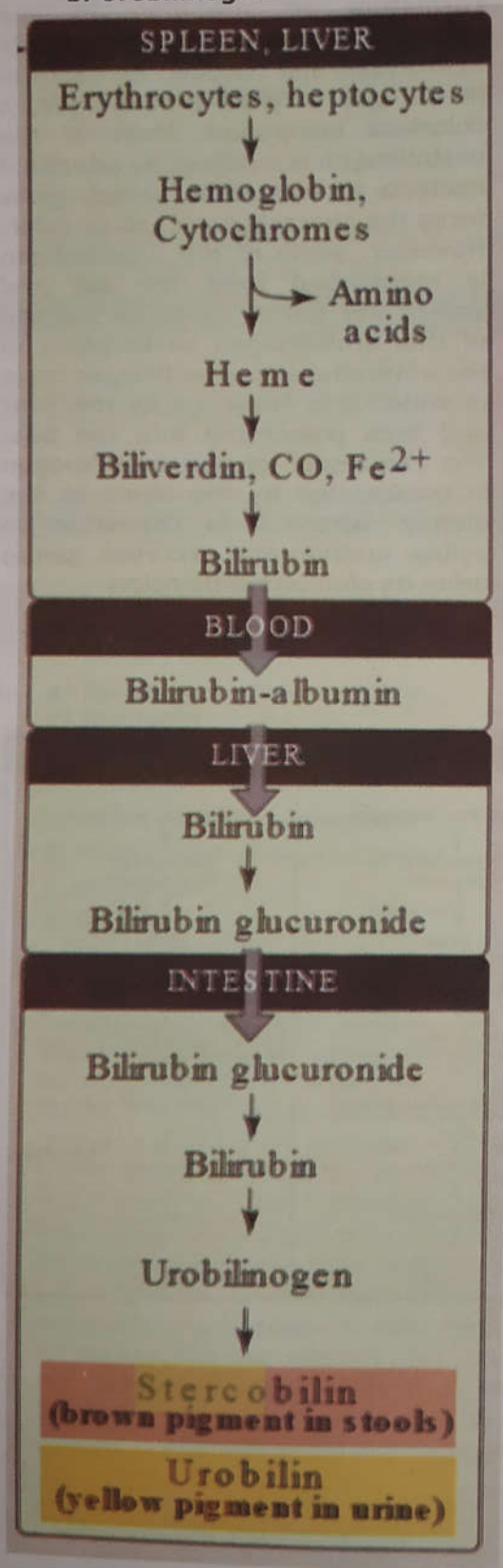


Formation of urobilins in the intestine: Bilirubin diglucuronide is hydrolyzed and reduced by bacteria in the gut to yield urobilinogen, a colorless compound. Most of the urobilinogen is oxidized by intestinal bacteria to stercobilin, which gives feces the characteristic brown color. However, some of the urobilinogen is reabsorbed from the gut and enters the portal blood. A portion of this urobilinogen participates in the enterohepatic urobilinogen cycle in which it is taken up by the liver and then resecreted into the bile. The remainder of the urobilinogen is transported by the blood to the kidney, where it is converted to yellow urobilin and excreted, giving urine its characteristic color.

Types of Jaundice:



b. Urobilinogen-



c. Mevobilirubin

d. Bilirubin

11. b) Converts a hydrophobic compound to a hydrophilic one

12: a) Hemoglobin b) Catalase d) Cytochrome e) Pyrolase

[Ref: Harper's Illustrated biochemistry, 28th Edition]

a. Hemoglobin - Porphyrins are cyclic compounds that readily bind metal ions, usually ferrous (Fe2+) or ferric (Fe3+) iron. The most prevalent metalloporphyrin in humans is heme, which consists of one Fe2+ coordinated in the center of the tetrapyrrole ring of protoporphyrin IX

b. Catalase-

METALLOPORPHYRINS & HEMOPROTEINS ARE IMPORTANT IN NATURE:

Porphyrins are cyclic compounds formed by the linkage of four pyrrole rings through methyne (— —HC—) bridges (Figure 31–1). A characteristic property of the porphyrins is the formation of complexes with metal ions bound to the nitrogen atom of the pyrrole rings. Examples are the iron porphyrins such as heme of hemoglobin and the magnesium-containing porphyrin chlorophyll, the photosynthetic pigment of plants. Proteins that contain heme (hemoproteins) are widely distributed in nature. Examples of their importance in humans and animals are listed in Table

Protein	Function
Hemoglobin	Transport of oxygen in blood
Myoglobin	Storage of oxygen in muscle
Cytochrome c	Involvement in electron transport chain
Cytochrome P450	Hydroxylation of xenobiotics
Catalase	Degradation of hydrogen peroxide
Tryptophan pyrrolase	Oxidation of tryptophan

c. Bilibrubin

d. Cytochrome-

Myoglobin, hemoglobin, cytochromes, and many other metalloproteins contain tightly associated metal ions.

e. Pyrolase

13. b) Histidine

a. Leucine

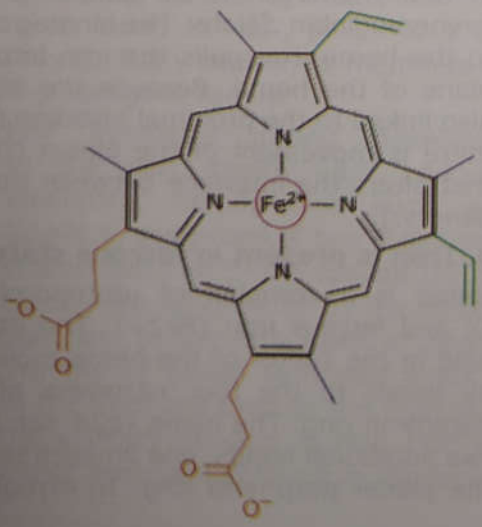
b.Histidine-

Myoglobin and hemoglobin contain heme, a cyclic tetrapyrrole consisting of four molecules of pyrrole linked by α-methylene bridges. This planar network of conjugated double bonds absorbs visible light and colors heme deep red. The substituents at the β-positions of heme are methyl (M), vinyl (V), and propionate (Pr) groups arranged in the order M, V, M, V, M, Pr, Pr, M .One atom of ferrous iron (Fe2+) resides at the center of the planar tetrapyrrole. Other proteins with metal-containing tetrapyrrole prosthetic groups include the cytochromes (Fe and Cu) and chlorophyll (Mg) . Oxidation and reduction of the Fe and Cu atoms of cytochromes are essential to their biologic function as carriers of electrons. By contrast, oxidation of the Fe2+ of myoglobin or hemoglobin to Fe3+ destroys their biologic activity.

The Iron Moves Toward the Plane of the Heme

When Oxygen Is Bound The iron of unoxygenated myoglobin lies 0.03 nm (0.3 Å) outside the plane of the heme ring, toward His F8. The heme therefore "puckers" slightly. When O2 occupies the sixth coordination position, the iron moves to within 0.01 nm (0.1 Å) of the plane of the heme ring. Oxygenation of myoglobin, thus, is accompanied by motion of the iron, of His F8, and of residues linked to His F8.

Heme.



The pyrrole rings and methylene bridge carbons are coplanar, and the iron atom (Fe2+) resides in almost the same plane. The fifth and sixth coordination positions of Fe2+ are directed perpendicular to—and directly above and below—the plane of the heme ring. Observe the nature of the methyl (blue), vinyl (green), and propionate (orange) substituent groups on the β carbons of the pyrrole rings, the central iron atom (red), and the location of the polar side of the heme ring (at about 7 o'clock) that faces the surface of the myoglobin molecule.

c. Isoleucine

d. Valine

14. c) Has an O2 dissociation curve that is unaffected by wide range of pH

[Ref: Harper's Illustrated biochemistry, 28th Edition]

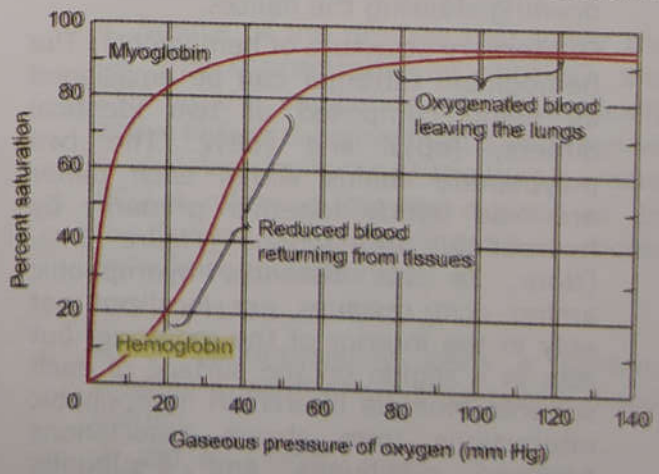
a. Contains four hemes per molecule

b. Shows the Bohr Effect

c.Has an O_2 dissociation curve that is unaffected by wide range of pH

The oxygen dissociation curves for myoglobin & hemoglobin suit their physiologic roles

Why is myoglobin unsuitable as an O2 transport protein but well suited for O2 storage? The relationship between the concentration, or partial pressure, of O2 (Po2) and the quantity of O2 bound is expressed as an O2 saturation isotherm



Oxygen-binding curves of both hemoglobin and myoglobin. Arterial oxygen tension is about 100 mm Hg;

mixed venous oxygen tension is about 40 mm Hg; capillary (active muscle) oxygen tension is about 20 mm Hg; and the minimum oxygen tension required for cytochrome oxidase is about 5 mm Hg. Association of chains into a tetrameric structure (hemoglobin) results in much greater oxygen delivery than would be possible with single chains.

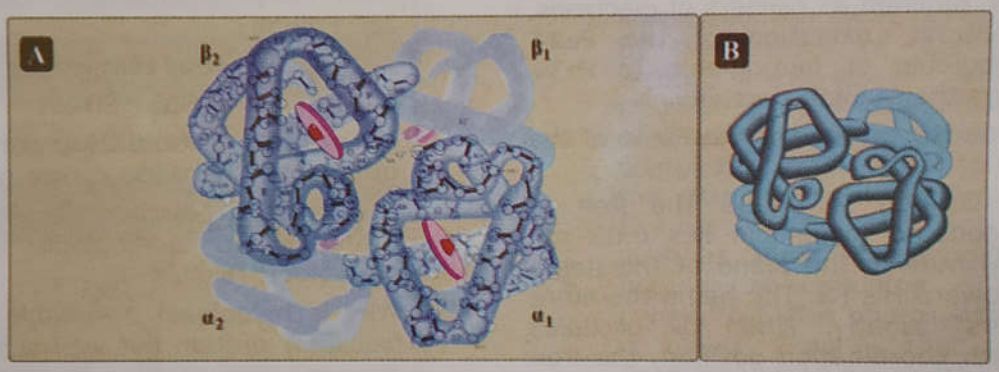
d. None of the above.

15. a) Hb has 2 polypeptide
c) Hb structurally similar to myoglobin

[Ref: Lippincott's illustrated reviews, 6th Edition]

a. Hb has 2 polypeptide-

Structure and function of hemoglobin Hemoglobin is found exclusively in red blood cells (RBC), where its main function is to transport oxygen (O2) from the lungs to the capillaries of the tissues. Hemoglobin A, the major hemoglobin in adults, is composed of four polypeptide chains (two α chains and two β chains) held together by noncovalent interactions. Each chain (subunit) has stretches of α-helical structure and a hydrophobic heme-binding pocket similar to that described for myoglobin. However, the tetrameric hemoglobin molecule is structurally and functionally more complex than myoglobin. For example, hemoglobin can transport H+ and CO2 from the tissues to the lungs and can carry four molecules of O2 from the lungs to the cells of the body. Furthermore, the oxygen-binding properties of hemoglobin are regulated by interaction with allosteric effectors.



A. Structure of hemoglobin showing the polypeptide backbone. B. Simplified drawing showing the helices.

Quaternary structure of hemoglobin: The hemoglobin tetramer can be envisioned as being composed of two identical dimers, (αβ)1 and (αβ)2. The two polypeptide chains within each dimer are held tightly together primarily by hydrophobic interactions (Figure 3.4). [Note: In this instance, hydrophobic amino acid residues are localized not only in the interior of the molecule, but also in a region on the surface of each subunit. Multiple interchain hydrophobic interactions form strong associations between α-subunits and β-subunits in the dimers.] In contrast, the two dimers are held together primarily by polar bonds. The weaker interactions between the dimers allows them to move with respect to one other. This movement results in the two dimers occupying different relative positions in deoxyhemoglobin as compared with oxyhemoglobin .[Note: The binding of O2 to the heme iron pulls the iron into the plane of the heme. Because the iron is also linked to the proximal histidine (F8), there is movement of the globin chains that alters the interface between the αβ dimers.]

b. Iron is present in ferrous state-

Heme is a complex of protoporphyrin IX and ferrous iron (Fe2+) .The iron is held in the center of the heme molecule by bonds to the four nitrogens of the porphyrin ring. The heme Fe2+ can form two additional bonds, one on each side of the planar porphyrin ring. In myoglobin

and hemoglobin, one of these positions is coordinated to the side chain of a histidine residue of the globin molecule, whereas the other position is available to bind oxygen.

c. Hb structurally similar to myoglobin-

hemoglobin is quaternary structure while myoglobin is tertiary.

d. Ferrous ions are in porphyrin rings

16. a) Decrease in pH
b) Increase in 2, 3 diphosphoglycerate concentration
c) Increase in $C0_2$ concentration

a. Decrease in pH-

b. Increase in 2, 3 diphosphoglycerate concentration-

c. Increase in $C0_2$ concentration

d. Increase in the partial pressure of 0_2

- Because 2,3-BPG decreases the O2 affinity of hemoglobin, a reduction in 2,3BPG should result in increased O2 affinity and decreased delivery of O2 to tissues. The relaxed form is the high-oxygen-affinity form of hemoglobin. Increased O2 affinity (decreased delivery) results in a left shift in the O2-dissociation curve. Decreased O2 delivery is compensated for by increased RBC production.

17. b) $alpha_2$ $epsilon_2$

a. $alpha$, $beta_2$

b.$alpha_2$ $epsilon_2$

Fetal hemoglobin: HbF is a tetramer consisting of two α chains identical to those found in HbA, plus two γ chains (α2γ2). The γ chains are members of the β-globin gene family.

HbF synthesis during development: In the first month after conception, embryonic hemoglobins such as Hb Gower 1, composed of two α-like zeta (ζ) chains and two β-like epsilon (ε) chains (ζ2ε2), are synthesized by the embryonic yolk sac. In the fifth week of gestation, the site of globin synthesis shifts, first to the liver and then to the marrow, and the primary product is HbF. HbF is the major hemoglobin found in the fetus and newborn, accounting for about 60% of the total hemoglobin in the RBC during the last months of fetal life.HbA synthesis starts in the bone marrow at about the eighth month of pregnancy and gradually replaces HbF. [Note: HbF represents less than 1% of the hemoglobin in most adults and is concentrated in RBC known as F cells.

c. $alpha_2$ gamma,

d. $alpha_1$ $epsilon_2$

18. b) Effect of PC02 on oxyhemoglobin dissociation

[Ref: Stryer 8th Edition]

a. Effect on Zn on carbonic anhydrase activity

b. Effect of $PC0_2$ on oxyhemoglobin dissociation-

Bohr effect: The release of oxygen from hemoglobin is enhanced when the pH is lowered or when the hemoglobin is in the presence of an increased pCO2. Both result in a decreased oxygen affinity of hemoglobin and, therefore, a shift to the right in the oxygen-dissociation curve (Figure 3.8), and both, then, stabilize the T (deoxy) form. This change in oxygen binding is called the Bohr effect. Conversely, raising the pH or lowering the concentration of CO2 results in a greater affinity for oxygen, a shift to the left in the oxygen-dissociation curve, and stabilization of the R (oxy) form.

a. Source of the protons that lower the pH: The concentration of both H+ and CO2 in the capillaries of metabolically active tissues is higher than that observed in alveolar capillaries of the lungs, where CO2 is released into the expired air. In the tissues, CO2 is converted by carbonic anhydrase to carbonic acid:

$CO_2 + H_2O \leftarrow\rightarrow H2CO3$

which spontaneously loses a proton, becoming bicarbonate (the major blood buffer):

$H_2CO_3 \leftarrow\rightarrow HCO_3^- + H^+$

The H+ produced by this pair of reactions contributes to the lowering of pH. This differential pH gradient (that is, lungs

having a higher pH and tissues a lower pH) favors the unloading of oxygen in the peripheral tissues and the loading of oxygen in the lung. Thus, the oxygen affinity of the hemoglobin molecule responds to small shifts in pH between the lungs and oxygen-consuming tissues, making hemoglobin a more efficient transporter of oxygen.

c. $HC0_3$ leaving the RBC in exchange of CI-

d. H leaving RBC for each $C0_2$ that inters

19. d) Subunits are held together by hydrogen bonds

[Ref: Stryer 8th Edition]

a. Non-helical

b. Subunits are held together by hydrogen bonds

c. Binds with 2 Heme

d. Heme at hydrophobic pockets-

Hydrophobic Interactions Hydrophobic interaction refers to the tendency of nonpolar compounds to self-associate in an aqueous environment. This self-association is driven neither by mutual attraction nor by what are sometimes incorrectly referred to as "hydrophobic bonds." Self-association minimizes energetically unfavorable interactions between nonpolar groups and water. While the hydrogens of nonpolar groups such as the methylene groups of hydrocarbons do not form hydrogen bonds, they do affect the structure of the water that surrounds them. Water molecules adjacent to a hydrophobic group are restricted in the number of orientations (degrees of freedom) that permit them to participate in the maximum number of energetically favorable hydrogen bonds.

Hemoglobin is found exclusively in red blood cells (RBC), where its main function is to transport oxygen (O2) from the lungs to the capillaries of the tissues. Hemoglobin A, the major hemoglobin in adults, is composed of four polypeptide chains (two α chains and two β chains) held together by noncovalent interactions. Each chain (subunit) has stretches of α-helical structure and a hydrophobic heme-binding pocket similar to that described for myoglobin. However, the tetrameric hemoglobin molecule is structurally and functionally more complex than myoglobin. For example, hemoglobin can transport H+ and CO2 from the tissues to the lungs and can carry four molecules of O2 from the lungs to the cells of the body. Furthermore, the oxygen-binding properties of hemoglobin are regulated by interaction with allosteric effectors .

e. Bind with 1 molecule of O2

20. c) Hb -> Heme ->biliverdin ->bilirubin ->urobilinogen

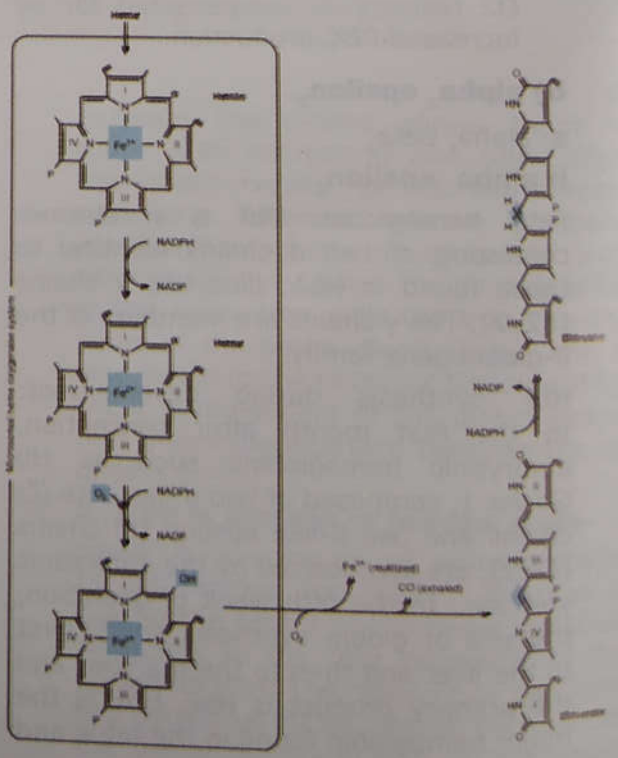
[Ref: Lippincott's illustrated reviews, 6th Edition & Stryer 8th Edition]

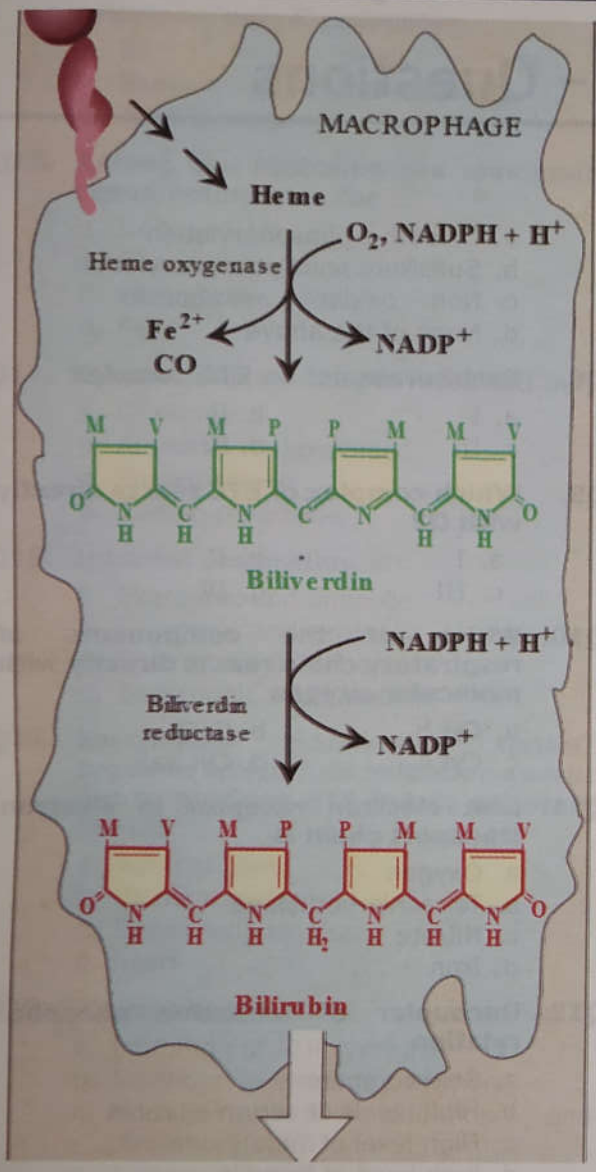
a. Hb -> Heme ->bilirubin ->urobilinogen

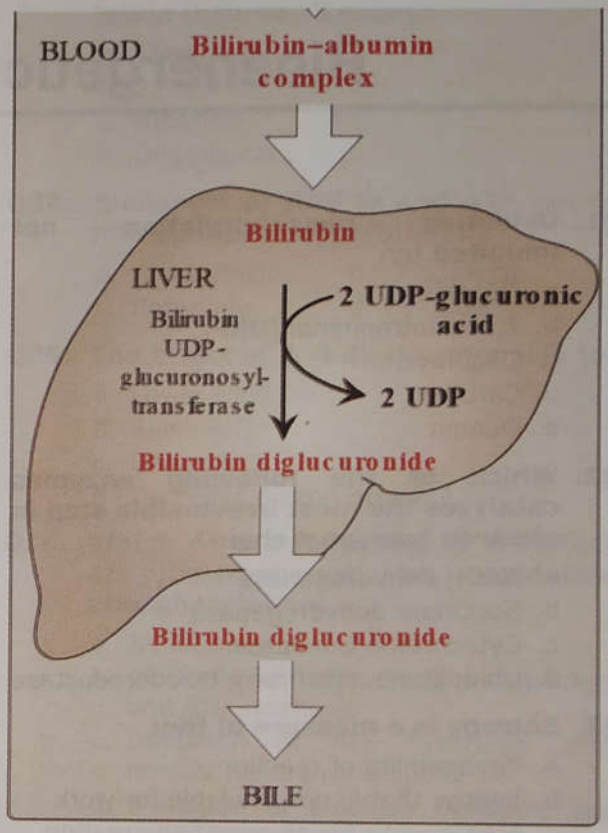
b. Heme->Hb -> biliverdin -> urobilinogen

c. Hb -> Heme ->biliverdin ->bilirubin ->urobilinogen

Schematic representation of the microsomal heme oxygenase system.







Formation of bilirubin from heme and its conversion to bilirubin diglucuronide

d.Hb->Heme ->bilirubin ->urobilingen ->biliverdin

Bioenergetics – Questions

Q1. Oxidative phosphorylation not inhibited by:

a. Fluoride
b. 2, 4-dinitrophenol (DNP)
c. Oligomycin
d. Carboxin
e. Ouabin

Q2. Which of the following enzymes catalyses the most irreversible step in electron transport chain?

a. NADH dehydrogenase
b. Succinate dehydrogenase
c. Cytochrome C oxidase
d. Ubiquinone cytochrome c oxidoreductase

Q3. Entropy is a measure of the:

a. Reversibility of reaction
b. Energy that is not available for work
c. Free energy for an enzymatic reation
d. Exothermicity

Q4. The mechanism of action of uncouplers of oxidative phosphorylation involves:

a. Inhibition of ATP synthase
b. Stimulation of ATP synthase
c. Disruption of proton gradient across the inner membrane
d. Disruption of proton gradient across membrane

Q5. Chemiosmotic coupling of oxidation phosphorylation is related to:

a. Formation of ATP at substrate level
b. ATP generation of pumping of proton
c. ATP generation of pumping of neutron
d. ATP formation by transport of O2

Q6. ATP is generated in ETC by:

a. Na + K + ATpase
b. Na+ CI –ATPase
c. FoF ATPase
d. ADP Kinase

Q7. Main source of ATP production is

a. Oxidative phosphorylation
b. Substrate level phosphorylation
c. Non – oxidative metabolism
d. None of the above

Q8. Barbiturate act on ETC complex

a. I b. II
c. III d. IV

Q9. Which complex of ETC reacts directly with O2

a. I b. II
c. III d. IV

Q10. Which of the components of respiratory chain reacts directly with molecular oxygen

a. Cyt b b. CoQ
c. Cyt C d. Cyt aa3

Q11. Last electron receptor in electron transport chain is

a. Oxygen
b. Tetrachloroethylene
c. Nitrate
d. Iron

Q12. Uncoupler of oxidative phosphorylation

a. Snake venom
b. High levels of serum bilirubin
c. High level of T4
d. high level of free F.A
e. All of the above

Q13. Cyanide is toxic because it

a. Inhibits cytochorme oxidase
b. Forms cyano meth Hemoglobin
c. Inhibits ATP carrier in mitochondria
d. Inhibits Na – K ATPase

Q14. The enzyme marker of electron transport system is

a. Cytochrome reductase
b. Fumarase
c. Pyruvate
d. Malate dehydrogenase

1. a, b, c	2. c	3. b	4. c	5. b	6. c	7. a	8. a	9. d	10. d
11. a	12. e	13. a	14. a						

Q15. Which of the following is a constituent of cytochrome C reducatse

a. B1 b. B2
c. Biotin d. Pyridoxine
e. Ascrobic acid

Q16. Among the following the maximum redox potential is for

a. NADH / NAD
b. Succinyl Co A fumarate
c. Ubiquinone
d. Fe2+

Q17. Cytochrome oxidase is inhibited by

a. Cyanide
b. Atuminium phosphide
c. Phenobartone
d. Carbon monoxide

Q18. Internal respiration is :

a. Exergonic and anabolic
b. Exergonic and catabolic
c. Endergonic and anabolic
d. Endergonic and catabolic

Q19. Specialized mammalian tissue/ organ in which fuel oxidation serves not to produce ATP but to generate heat is

a. Adernal gland
b. Skeletal muscle
c. Brown adipose tissue
d. heart

Q20. Dinitrophenol cause

a. Inhibition of ATP synthase
b. Inhibition of electron transport
c. Uncoupling of oxidation and phosphorylation
d. Accumulation of ATP

Q21. Which component transfers four protons?

a. NADH- Q oxidoreductase
b. Cytochrome oxidase
c. Coenz Q - Cytochrome C oxidoreductase
d. Isocitrate dehydrogenase
e. Succinate Q reductase

Q22. Which of the following is an uncoupler?

a. Insulin b. Epinephrine
c. GH d. Thyroxine

Q23. Uncouplers of Oxidative phosphorylation include all except

a. Thermogenin
b. 2, 4 Di-nitrophenol
c. Nigericin
d. Oligomycin

Q24. Transport of ADP in and ATP out of mitochondria is inhibited by

a. Atractyloside b. Oligomycin
c. Rotenone d. Cyanide

Q25. The effect of 2, 4 dinitrophenol is to:

a. Lower BMR
b. Raise R,Q
c. Lower R.Q
d. Decrease proton gradient -

Q26. Which of the following is an effect of dinitrophenol on oxidative phosphorylation:

a. Inhibtion of cytochrome b
b. Blockade of both electron transport and ATP synthesis
c. Inhibition of ATP synthesis with normal electron transport
d. Inhibition of electron transport but not ATP synthesis

Q27. Cytochrome oxidase contains:

a. Ca++ b. Cu
c. Mn d. Zn

Q28. The following poisons act by causing inhibition of complex IV of respiratory chain except-

a. Cyanide b. Malonate
c. H2S d. CO

Q29. The number of ATP molecules produce for each molecules of FADH2 oxidized via the respiratory chain is:

a. 1 b. 2.5
c. 1.5 d. 2

Q30. A child to emergency with accidental ingestion of Cyanide. It blocks citric acid cycle by blocking:

a. Acetyl-CoA Production
b. Aconitase
c. NAD+
d. Citrate

15. b	16. d	17. b	18. all	19. c	20. c	21. a	22. d	23. d	24. a
25. d	26. c	27. b	28. b	29. c	30. c				

Bioenergetics – Explanations

1. a) Fluoride
d) Carboxin
e) Ouabin

[Ref: Harper 30th Edition]

a. Fluoride- Enolase is inhibited by fluoride, and when blood samples are taken for measurement of glucose, glycolysis is inhibited by taking the sample into tubes containing fluoride.

b. 2, 4-dinitrophenol (DNP)-

The uncouplers allow Electron Transport Chain to Occur without ATP formation:

- 2,4-dinitrophenol (DNP)
- Dinitrocresol
- Trifluorocarbonylcyanide phenylhydrazone
- Pentachlorophenol
- Antibiotics-valinomycin, gramicidin A and nigercin
- Aspirin (in high dose)
- **Physiological Uncouplers:**
  - Excessive thyroxine hormone
  - EFA deficiency
  - Long chain FA in Brown adipose tissue
  - Unconjugated hyperbilirubinaemia.

c. Oligomycin - Inhibits oxidative phosphorylation

d. Carboxin-Inhibits Complex II

e. Ouabin-Ouabain is a cardiac glycoside that acts by inhibiting the Na+/K+-ATPase sodium-potassium ion pump

2. c) Cytochrome C oxidase

[Ref: Harper 30th Edition]

- In electron transport chain, components are arrange from negative redox potential to positive redox potential.
- Redox potential is the tendency of a redox couple to accept or loose electron.
- A negative redox potential indicates the tendency to loose electron. e.g., NADH gives away its electron in ETC.
- A positive redox potential indicates the tendency to accept electron, e.g., Oxygen is the final acceptor of electron in the ETC.

System	E'_0 Volts
H^+/H_2	-0.42
NAD^+/NADH	-0.32
Lipoate; ox/red	-0.29
Acetoacetate/3-hydroxybutyrate	-0.27
Pyruvate/lactate	-0.19
Oxaloacetate/malate	-0.17
Fumarate/succinate	+0.03
Cytochrome b; Fe^{3+}/Fe^{2+}	+0.08
Ubiquinone; ox/red	+0.10
Cytochrome c_1;Fe^{3+}/Fe^{2+}	+0.22
Cytochrome a;Fe^{3+}/Fe^{2+}	+0.29
Oxygen/water	+0.82

a. NADH dehydrogenase-delivers its electrons to complex I and is not the most irreversible step as can be seen from the redox potentials.

b. Succinate dehydrogenase- delivers its electrons to complex II and is not the most irreversible step as can be seen from the redox potentials.

c. Cytochrome C oxidase-Cytochrome c oxidase catalyses the reduction of oxygen to water. So this is the most Irreversible reaction of ETC.

d. Ubiquinone cytochrome c oxidoreductase- delivers its electrons across complex III and is not the most irreversible step.

3: b) Energy that is not available for work

[Ref: Harper 30th Edition]

a. Reversibility of reaction-

A balanced chemical equation lists the initial chemical species (substrates) present and the new chemical species (products) formed for a particular chemical reaction, all in their respective proportions or stoichiometry. For example, balanced equation (1) indicates that one molecule

each of substrates A and B react to form one molecule each of products P and Q:

$A + B \leftrightarrows P + Q$

The double arrows indicate reversibility, an intrinsic property of all chemical reactions. Thus, for reaction (1), if A and B can form P and Q, then P and Q can also form A and B. Designation of a particular reactant as a "substrate" or "product" is therefore somewhat arbitrary since the products for a reaction written in one direction are the substrates for the reverse reaction. The term "products" is, however, often used to designate the reactants whose formation is thermodynamically favored. Reactions for which thermodynamic factors strongly favor formation of the products to which the arrow points often are represented with a single arrow as if they were "irreversible":

$A + B \rightarrow P + Q$

b. Energy that is not available for work-

Entropy is the extent of disorder or randomness of the system and becomes maximum as equilibrium is approached. Under conditions of constant temperature and pressure, the relationship between the free-energy change (ΔG) of a reacting system and the change in entropy (ΔS) is expressed by the following equation, which combines the two laws of thermodynamics:

$\Delta G = \Delta H - T\Delta S$

where ΔH is the change in enthalpy (heat) and T is the absolute temperature.

c. Free energy for an enzymatic reation-

The Gibbs free energy change ΔG (also called either free energy or Gibbs energy) describes in quantitative form both the direction in which a chemical reaction will tend to proceed and the concentrations of reactants and products that will be present at equilibrium.

ΔG for a chemical reaction equals the sum of the free energies of formation of the reaction products ΔG_p minus the sum of the free energies of formation of the substrates ΔG_s. A similar but different quantity designated by ΔG^0 denotes the change in free energy that accompanies transition from the standard state, one-molar concentrations of substrates and products, to equilibrium. A more useful biochemical term is $\Delta G^{0'}$, which defines ΔG^0 at a standard state of 10^{-7} M protons, pH 7.0. If the free energy of formation of the products is lower than that of the substrates, the signs of ΔG^0 and $\Delta G^{0'}$ will be negative, indicating that the reaction as written is favored in the direction left to right. Such reactions are referred to as spontaneous. The sign and the magnitude of the free energy change determine how far the reaction will proceed.

ΔG^0: $\Delta G^0 = -RT \ln Keq$, illustrates the relationship between the equilibrium constant Keq.

where R is the gas constant (1.98 cal/mol°K or 8.31 J/mol°K) and T is the absolute temperature in degrees Kelvin. Keq is equal to the product of the concentrations of the reaction products, each raised to the power of their stoichiometry, divided by the product of the substrates, each raised to the power of their stoichiometry: For the reaction:

For the reaction $A + B \rightleftarrows P + Q$

$$K_{eq} = \frac{[P][Q]}{[A][B]}$$

ΔG^0 may be calculated from equation if the molar concentrations of substrates and products present at equilibrium are known.

If ΔG^0 is a negative number, Keq will be greater than unity, and the concentration of products at equilibrium will exceed that of the substrates.

If ΔG^0 is positive, Keq will be less than unity, and the formation of substrates will be favored.

Note that, since ΔG^0 is a function exclusively of the initial and final states of the reacting species, it can provide information only about the direction and equilibrium state of the reaction.

ΔG^0 is independent of the mechanism of the reaction, and provides no information concerning rates of reactions.

d. Exothermicity-

The terms exergonic and endergonic, rather than the normal chemical terms "exothermic" and "endothermic," are used to indicate that a process is accompanied by loss or gain, respectively, of free energy in any form, not necessarily as heat. In practice, an endergonic process cannot exist independently, but must be a component of a coupled exergonic endergonic system

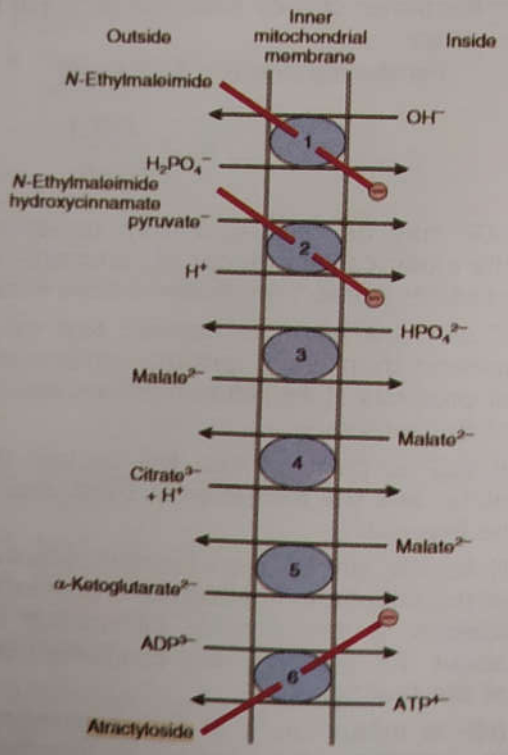
where the overall net change is exergonic. The exergonic reactions are termed catabolism (generally, the breakdown or oxidation of fuel molecules), whereas the synthetic reactions that build up substances are termed anabolism. The combined catabolic and anabolic processes constitute metabolism

4. c) Disruption of proton gradient across the inner membrane

[Ref: Harper 30th Edition]

a. inhibition of ATP synthase-

Atractyloside inhibits oxidative phosphorylation by inhibiting the transporter of ADP into and ATP out of the mitochondrion .The antibiotic oligomycin completely blocks oxidation and phosphorylation by blocking the flow of protons through ATP synthase .



Transporter systems in the inner mitochondrial membrane

b. Stimulation of ATP synthase –This is not the mechanism of uncouplers.

c. Disruption of proton gradient across the inner membrane –

Uncouplers dissociate oxidation in the respiratory chain from phosphorylation. These compounds are toxic in vivo, causing respiration to become uncontrolled, since the rate is no longer limited by the concentration of ADP or Pi. The uncoupler that has been used most frequently is 2,4-dinitrophenol, but other compounds act in a similar manner. Thermogenin (or the uncoupling protein) is a physiological uncoupler found in brown adipose tissue that functions to generate body heat, particularly for the newborn and during hibernation in animals .

d. Disruption of proton gradient across membrane –ans c is more specific

5. b) ATP generation of pumping of proton

[Ref: Harper 30th Edition]

a. Formation of ATP at substrate level-Formation of ATP at Oxidative Phosphorylation and not at substrate level Phosphorylation.

b. ATP generation of pumping of proton –

The flow of electrons through the respiratory chain generates ATP by the process of oxidative phosphorylation. The chemiosmotic theory, proposed by Peter Mitchell in 1961, postulates that the two processes are coupled by a proton gradient across the inner mitochondrial membrane so that the proton motive force caused by the electrochemical potential difference (negative on the matrix side) drives the mechanism of ATP synthesis. As we have seen, Complexes I, III, and IV act as proton pumps. Since the inner mitochondrial membrane is impermeable to ions in general and particularly to protons, these accumulate in the intermembrane space, creating the proton motive force predicted by the chemiosmotic theory.

c. ATP generation of pumping of neutron-It is generation of protons and not neutrons.

d. ATP formation by transport of O2-It is accompanied by generation of protons

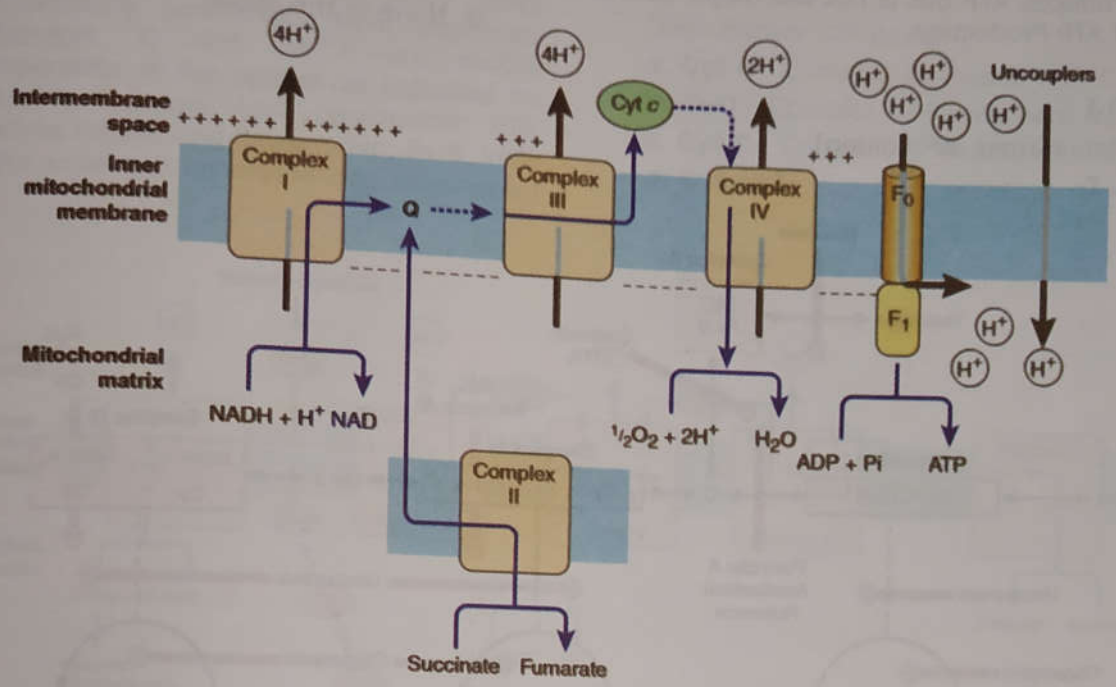
6. c) FoF ATPase

[Ref: Harper 30th Edition]

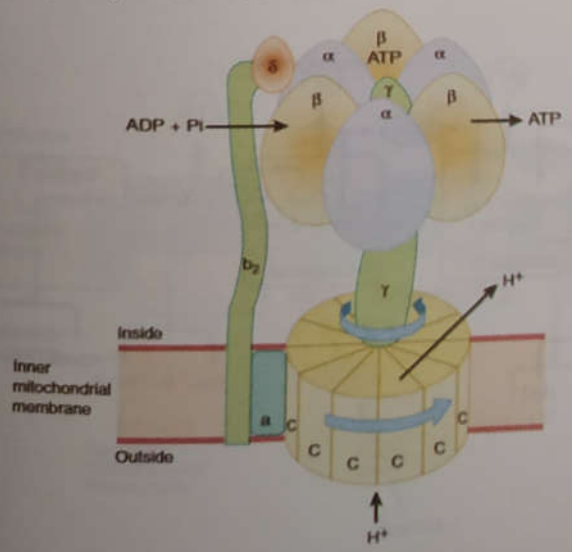
a. Na + K + ATpase-this is not a part of ETC.

b. Na+ CI –ATPase- this is not a part of ETC.

c. FoF1 ATPase-



A Membrane-Located ATP Synthase Functions as a Rotary Motor to Form ATP The proton motive force drives a membrane-located ATP synthase that forms ATP in the presence of Pi + ADP. ATP synthase is embedded in the inner membrane, together with the respiratory chain complexes .Several subunits of the protein form a ball-like shape arranged around an axis known as F1, which projects into the matrix and contains the phosphorylation mechanism.



F1 is attached to a membrane protein complex known as F0, which also consists of several protein subunits. F0 spans the membrane and forms a proton channel. The flow of protons through F0 causes it to rotate, driving the production of ATP in the F1 complex. This is thought to occur by a binding change mechanism in which the conformation of the β-subunits in F1 is changed as the axis rotates from one that binds ATP tightly to one that releases ATP and binds ADP and Pi so that the next ATP can be formed. Estimates suggest that for each NADH oxidized, Complexes I and III translocate four protons each and Complex IV translocates two.

d. ADP Kinase- this is not a part of ETC.

7. a) Oxidative phosphorylation

[Ref: Harper 30th Edition]

a. Oxidative phosphorylation-

Complexes I, III, and IV act as proton pumps creating a proton gradient across the membrane, which is negative on the matrix side. The proton motive force generated drives the synthesis of ATP as the protons flow back into the matrix through the ATP synthase enzyme.

b. Substrate level phosphorylation – Produces ATP but is not the major source of ATP Production.

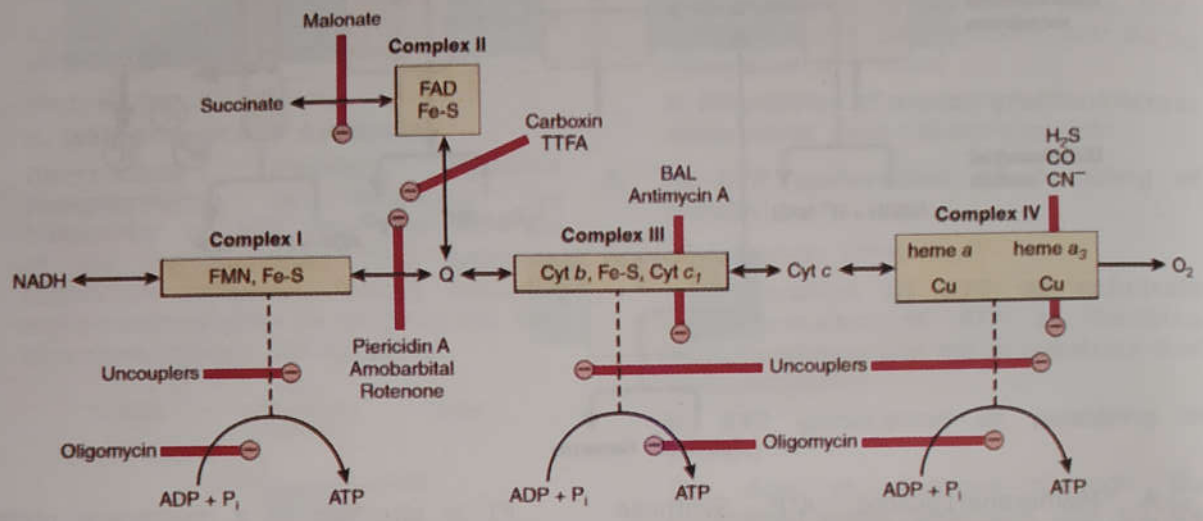
c. Non – oxidative metabolism-No ATP Production occurs

d. None of the above

8. a) I

[Ref: Harper 30th Edition]

a. I-



Barbiturates such as amobarbital inhibit electron transport via Complex I by blocking the transfer from Fe-S to Q. At sufficient dosage, they are fatal in vivo.

b. II-Not inhibited by Barbiturates.

c. III- Not inhibited by Barbiturates.

d. IV- Not inhibited by Barbiturates.

9: d. IV

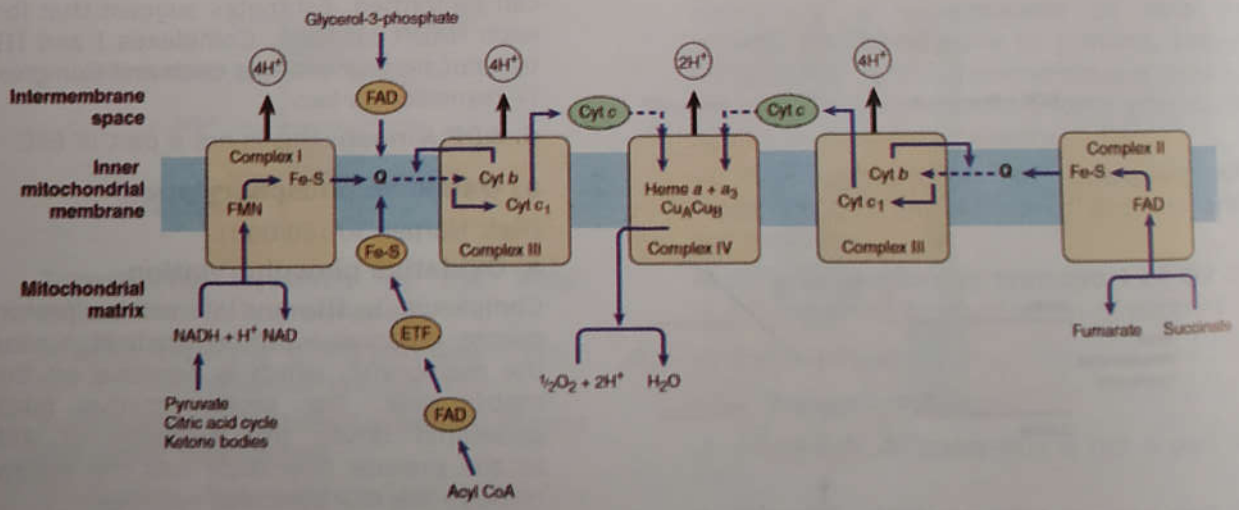
[Ref: Harper 30th Edition]

a. I-Complex IV Reacts with O_2

b. II-Complex IV Reacts with O_2

c. III-Complex IV Reacts with O_2

d. IV-



Flow of electrons through the respiratory chain complexes, showing the entry points for reducing equivalents from important substrates. Q and cyt c are mobile components of the system as indicated by the dotted arrows. (cyt, cytochrome; ETF, electron transferring flavoprotein; Fe-S, iron-sulfur protein; Q, coenzyme Q or ubiquinone.)

10. d) Cyt aa3

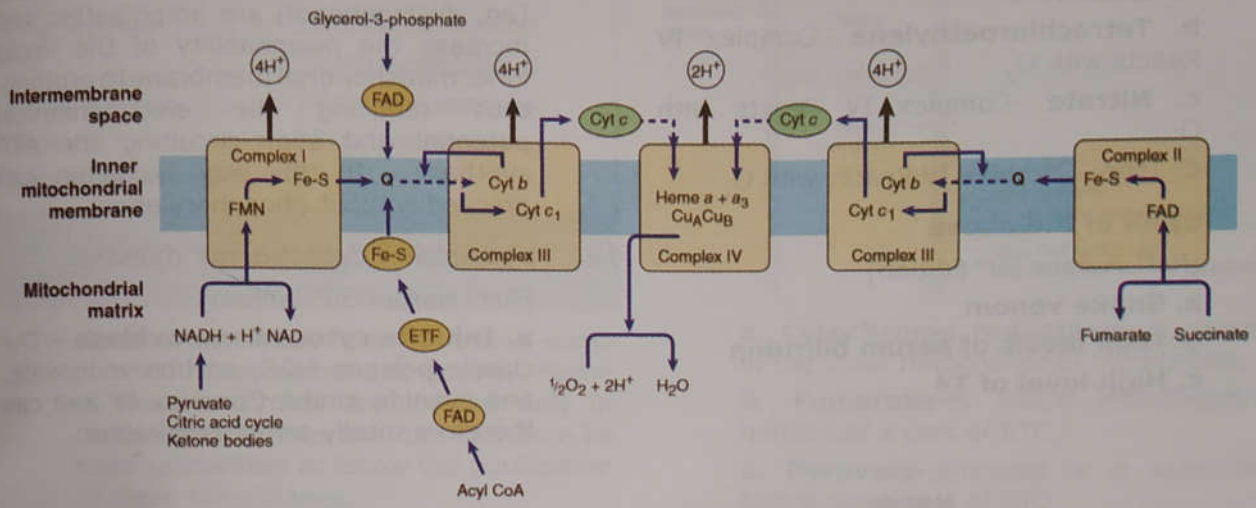
[Ref: Harper 30th Edition]

a. Cyt b - Complex IV Reacts with O_2

b. CoQ - Complex IV Reacts with O_2

c. Cyt C - Complex IV Reacts with O_2

d. Cyt aa3-



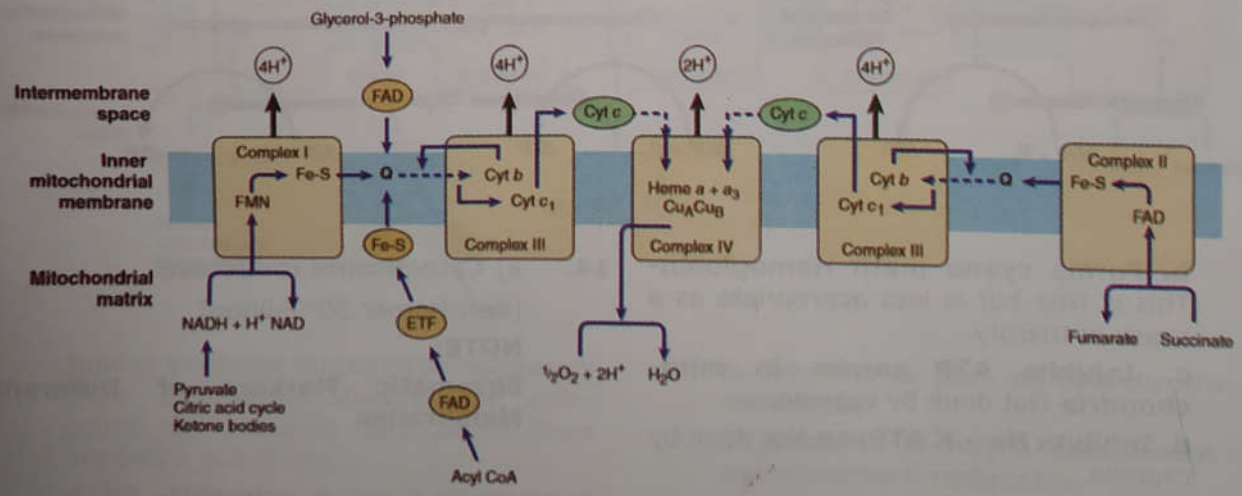
Flow of electrons through the respiratory chain complexes, showing the entry points for reducing equivalents from important substrates. Q and cyt c are mobile components of the system as indicated by the dotted arrows. (cyt, cytochrome; ETF, electron transferring flavoprotein; Fe-S, iron-sulfur protein; Q, coenzyme Q or ubiquinone.)

As can be seen Cyt aa3 are part of complex IV

11. a) Oxygen

[Ref: Harper 30th Edition]

a. Oxygen-



Flow of electrons through the respiratory chain complexes, showing the entry points for reducing equivalents from important substrates. Q and cyt c are mobile components of the system as indicated by the dotted arrows. (cyt, cytochrome; ETF, electron transferring flavoprotein; Fe-S, iron-sulfur protein; Q, coenzyme Q or ubiquinone.)

As can be seen Cyt a a3 are part of complex IV

b. Tetrachloroethylene -Complex IV Reacts with O_2

c. Nitrate -Complex IV Reacts with O_2

d. Iron -Complex IV Reacts with O_2

12. e) All of the above

[Ref: Harper 30th Edition]

a. Snake venom

b. High levels of serum bilirubin

c. High level of T4

d. High level of free F.A

e. All of the above-

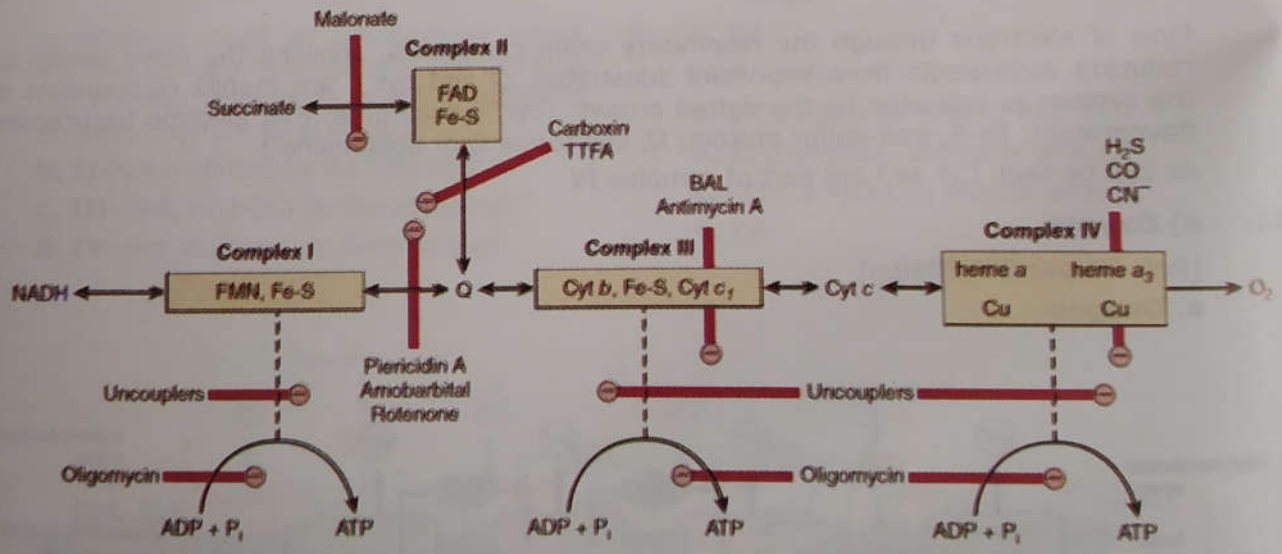
Ionophores Permit Specific Cations to Penetrate Membranes

Ionophores are lipophilic molecules that complex specific cations and facilitate their transport through biologic membranes, for example, valinomycin (K+). The classic uncouplers such as dinitrophenol are, in fact, proton ionophores.Uncouplers (eg, dinitrophenol) are amphipathic and increase the permeability of the lipoid inner mitochondrial membrane to protons, thus reducing the electrochemical potential and short-circuiting the ATP synthase . In this way, oxidation can proceed without phosphorylation.

13. a) Inhibits cytochorme oxidase

[Ref: Harper 30th Edition]

a. Inhibits cytochorme oxidase - The classic poisons H2S, carbon monoxide, and cyanide inhibit Complex IV and can therefore totally arrest respiration.



b. Forms cyano meth Hemoglobin- This is true but is less appropriate as a cause of toxicity.

c. Inhibits ATP carrier in mitochondria-Not done by cyanide.

d. Inhibits Na – K ATPase-Not done by cyanide.

14. a) Cytochrome reductase

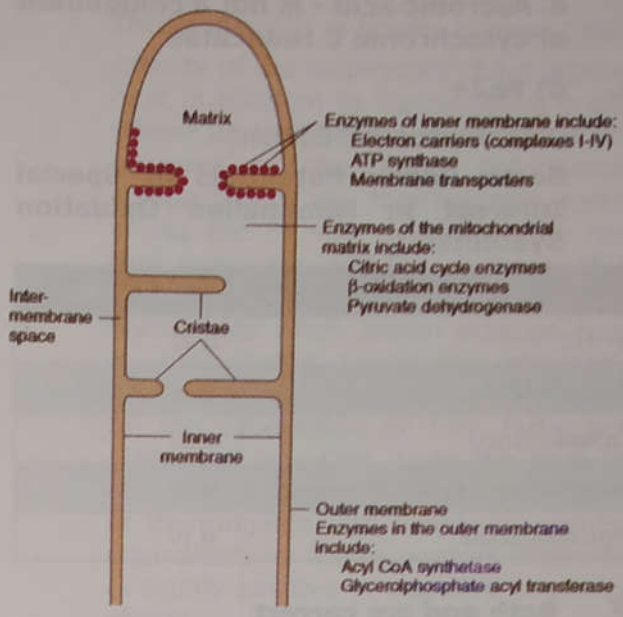
[Ref: Harper 30th Edition]

NOTE:

Enzymatic Markers of Different Membranes

Msembrane	Enzyme
Plasma	5'Nucleotidase Adenylyl cyclase NaH-K+-ATPase
Endoplasmic reticulum	Glucose-6-phosphatase
Golgi apparatus Cis Medial Trans Trans Golgi Network	GlcNAc transferase 1 Golgi mannosidase II Galactosyl transferase Sialyl transferase
Inner mitochondrial membrane	ATP synthase

Membranes contain many proteins, some of which have enzymatic activity. Some of these enzymes are located only in certain membranes and can therefore be used as markers to follow the purification of these membranes.



a. Cytochrome reductase- is present in the inner mitochondrial membrane.

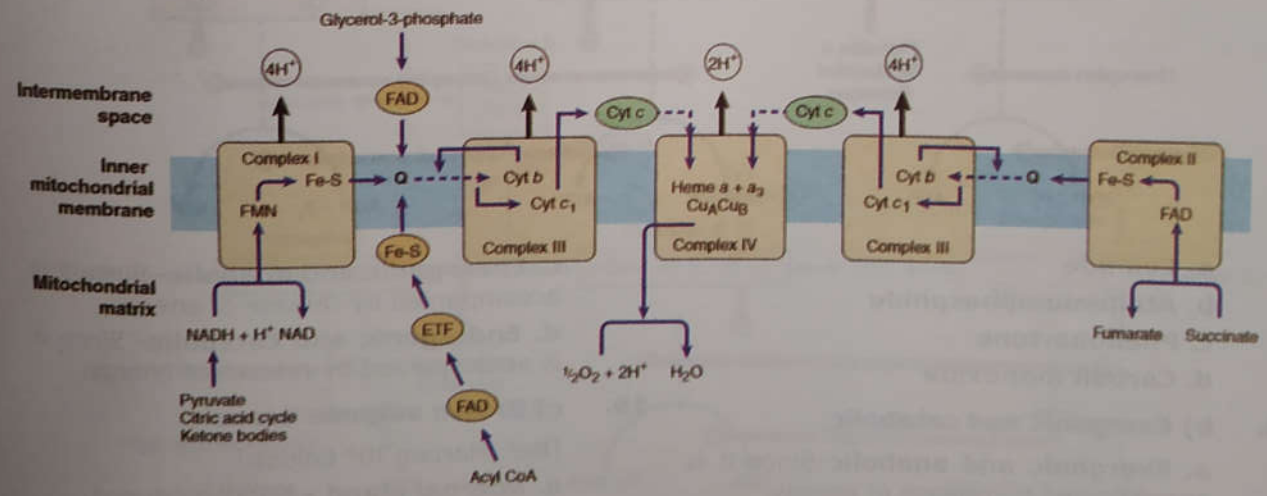
b. Fumarase-is inside mitochondria, hence not a part of ETC.

c. Pyruvate-pyruvate is a substrate, hence not a part of ETC.

d. Malate dehydrogenase- is inside mitochondria ,hence not a part of ETC.

15. b) B2-This is part of cytochrome C reducatse

[Ref: Harper 30th Edition]



Flow of electrons through the respiratory chain complexes, showing the entry points for reducing equivalents from important substrates.

a. B1 -Thiamine is not a component of cytochrome C reducatse

b. B2-This is part of cytochrome C reducatse

c. Biotin - is not a component of cytochrome C reducatse

d. Pyridoxine -is not a component of cytochrome C reducatse

e. Ascrobic acid - is not a component of cytochrome C reducatse

16. d) Fe2+

[Ref: Harper 30th Edition]

Some Redox Potentials of Special Interest in Mammalian Oxidation Systems:

System	E'0 Volts
H+/H2	-0.42
NADVNADH	-0.32
Lipoate; ox/red	-0.29
Acetoacetate/3-hydroxybutyrate	-0.27
Pyruvate/lactate	-0.19
Oxaloacetate/malate	-0.17
Fumarate/succinate	+0.03
Cytochrome b; Fe37Fe3+	+0.08
Ubiquinone; ox/red	+0.10
Cytochrome c; Fe34/Fe2+	+0.22
Cytochromes; Fe37Fe3+	+0.29
Oxygen/water	+0.82

a. NADH / NAD

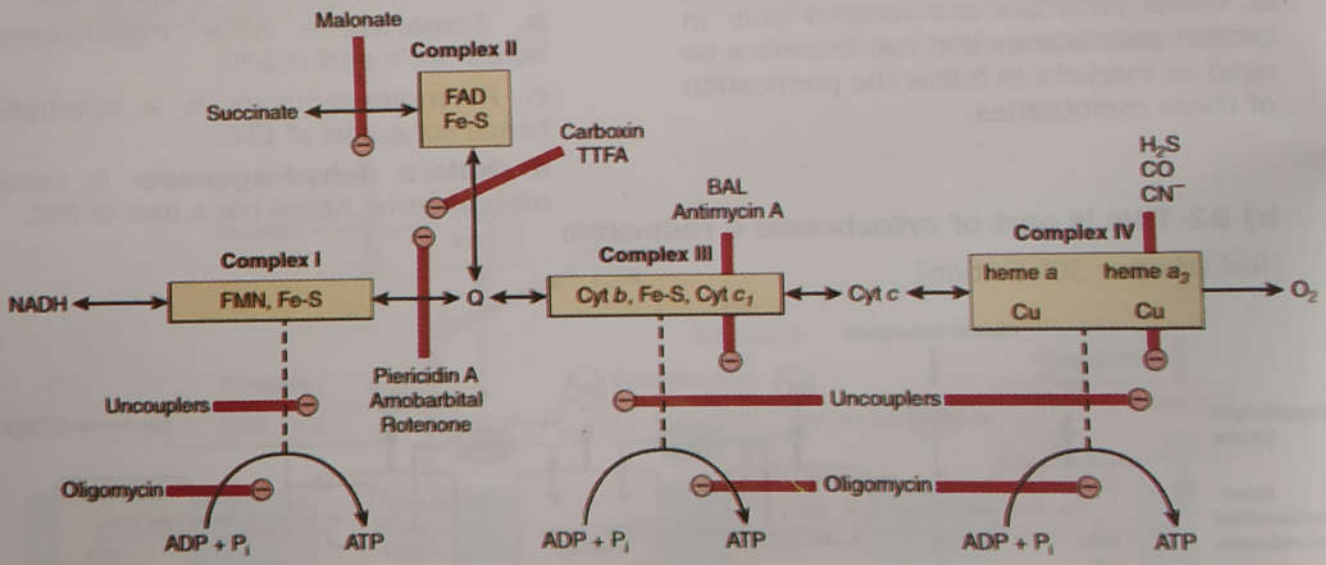
b. Succinyl Co A/ fumarate

c. Ubiquinone

d. Fe2+ -as can be seen Fe^{2+} has highest redox potential.

17. Both and are correct

[Ref: Harper 30th Edition]



a. Cyanide

b. Atuminiumphosphide

c. Phenobartone

d. Carbon monoxide

18. b) Exergonic and catabolic

a. Exergonic and anabolic-Since it is accompanied by release of energy.

b. Exergonic and catabolic- The exergonic reactions are termed catabolism (generally, the breakdown or oxidation of fuel molecules), whereas the synthetic reactions that build up substances are termed anabolism. The combined catabolic and anabolic processes constitute metabolism.

c. Endergonic and anabolic- Since it is accompanied by release of energy.

d. Endergonic and catabolic- Since it is accompanied by release of energy.

19. c) Brown adipose tissue

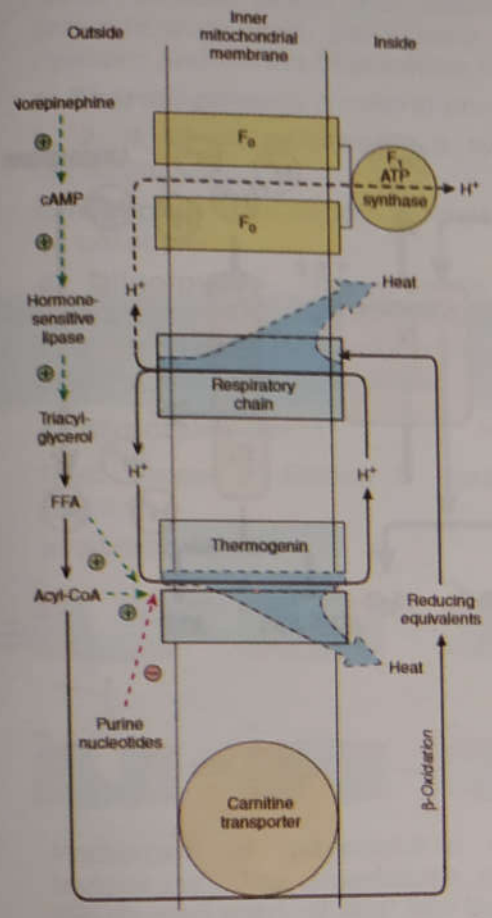
[Ref: Harper 30th Edition]

a. Adernal gland –ATP is produced.

b. Skeletal muscle–ATP is produced.

c. Brown adipose tissue-

Thermogenin (or the uncoupling protein) is a physiological uncoupler found in brown adipose tissue that functions to generate body heat, particularly for the newborn and during hibernation in animals.



Thermogenesis in brown adipose tissue:

Activity of the respiratory chain produces heat in addition to translocating protons .These protons dissipate more heat when returned to the inner mitochondrial compartment via thermogenin instead of via the F1 ATP synthase, the route that generates ATP.The passage of H+ via thermogenin is inhibited by purine nucleotides when brown adipose tissue is unstimulated. Under the influence of norepinephrine, the inhibition is removed by the production of free fatty acids (FFA) and acyl-CoA. Note the dual role of acyl-CoA in both facilitating the action of thermogenin and supplying reducing equivalents for the respiratory chain. and ⊖ signify positive or negative regulatory effects

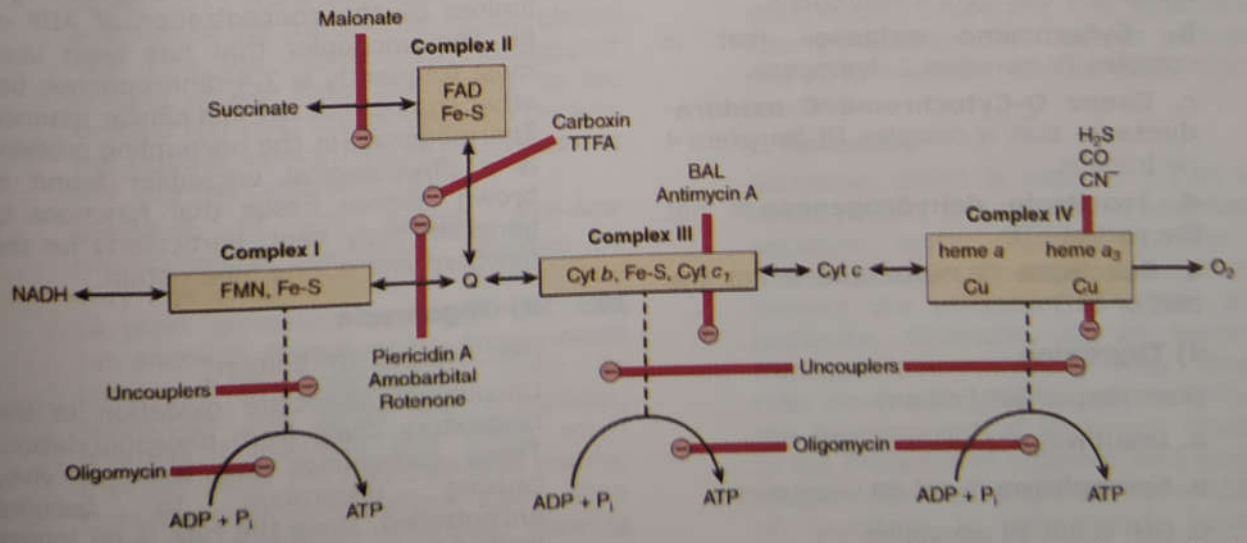
d. Heart -ATP is produced.

20. c) Uncoupling of oxidation and phosphorylation

[Ref: Harper 30th Edition]

a. Inhibition of ATP synthase-This is done by atractyloside.

b. Inhibition of electron transport-by inhibitors of ETC.



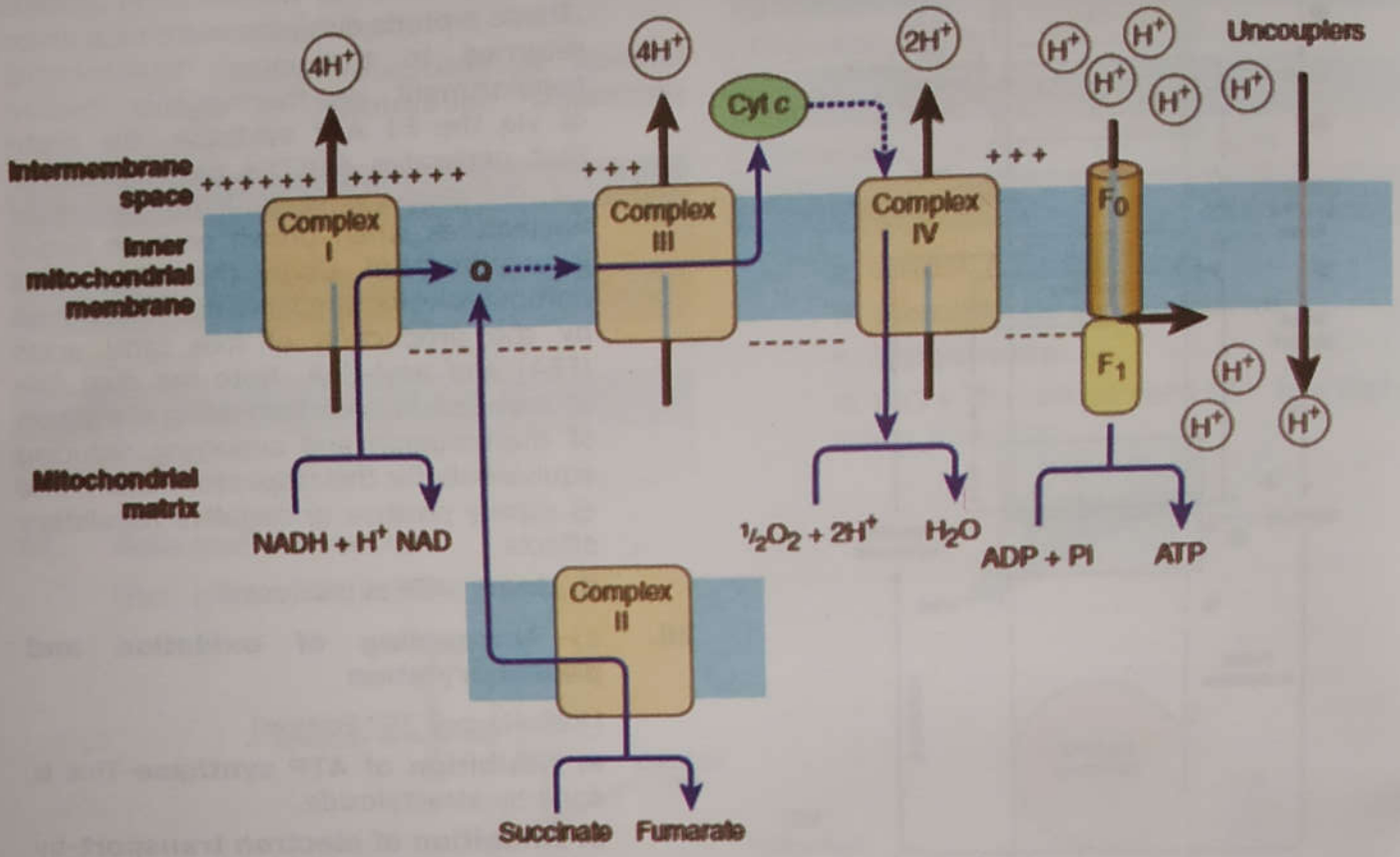
c. Uncoupling of oxidation and phosphorylation –

Uncouplers dissociate oxidation in the respiratory chain from phosphorylation. These compounds are toxic in vivo, causing respiration to become uncontrolled, since the rate is no longer limited by the concentration of ADP or Pi. The uncoupler that has been used most frequently is 2,4-dinitrophenol, but other compounds act in a similar manner.

d. Accumulation of ATP-this does not happen.

21. a) NADH- Q oxidoreductase

[Ref: Harper 30th Edition]



a. NADH- Q oxidoreductase-that is complex I transfers 4 Hydrogens.

b. Cytochrome oxidase- that is complex IV transfers 2 Hydrogens.

c. Coenz Q-Cytochrome C oxidoreductase- that is complex III transfers 4 Hydrogens.

d. Isocitrate dehydrogenase-is not the part of ETC.

e. Succinate Q reductase-is not the part of ETC.

22. d) Thyroxine

[Ref: Harper 30th Edition]

a. Insulin-is not an uncoupler

b. Epinephrine-is not an uncoupler

c. GH- is not an uncoupler

d. Thyroxine-

Uncouplers dissociate oxidation in the respiratory chain from phosphorylation. These compounds are toxic in vivo, causing respiration to become uncontrolled, since the rate is no longer limited by the concentration of ADP or Pi. The uncoupler that has been used most frequently is 2,4-dinitrophenol, but other compounds act in a similar manner. Thermogenin (or the uncoupling protein) is a physiological uncoupler found in brown adipose tissue that functions to generate body heat, particularly for the newborn and during hibernation.

23. d) Oligomycin

[Ref: Harper 30th Edition]

Uncouplers dissociate oxidation in the respiratory chain from phosphorylation. These compounds are toxic in vivo, causing respiration to become uncontrolled, since the rate is no longer limited by the concentration of ADP or Pi. The uncoupler that has been used most frequently is 2,4-dinitrophenol, but other compounds act in a similar manner. Thermogenin (or the uncoupling protein) is a physiological uncoupler found in

brown adipose tissue that functions to generate body heat, particularly for the newborn and during hibernation in .

a. Thermogenin-is a natural uncoupler.

b. 2, 4 Di-nitrophenol-is a synthetic uncoupler.

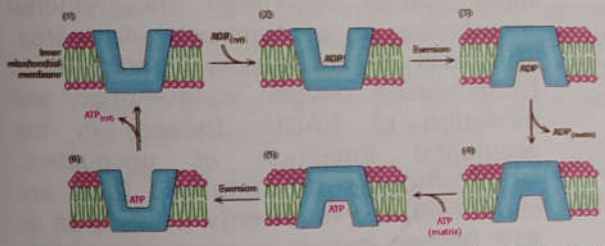
c. Nigericin-is an antiobiotic that acts as an uncoupler.

d. Oligomycin- The antibiotic oligomycin completely blocks oxidation and phosphorylation by blocking the flow of protons through ATP synthase .

24. a) Atractyloside

[Ref: Stryer 8th Edition & Harper 30th Edition]

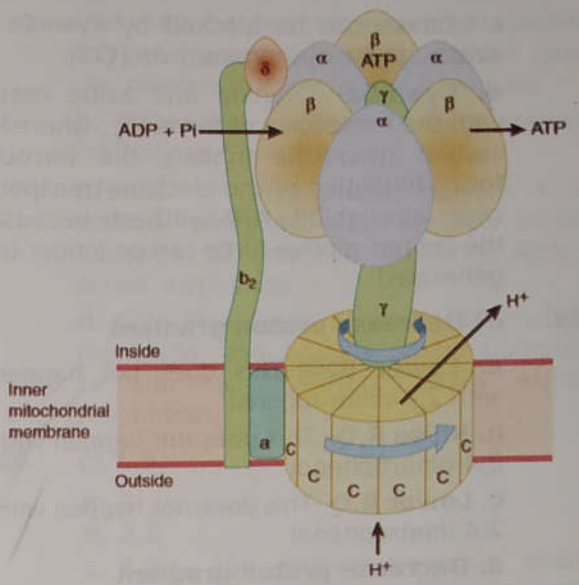
a. Atractyloside-



Mechanism of mitochondrial ATP-ADP translocase. The translocase catalyzes the coupled entry of ADP into the matrix and the exit of ATP from it. The binding of ADP (1) from the cytoplasm favors eversion of the transporter (2) to release ADP into the matrix (3). Subsequent binding of ATP from the matrix to the everted form (4) favors eversion back to the original conformation (5), releasing ATP into the cytoplasm (6).

Inhibition of ATP export. ATP-ADP translocase is specifically inhibited by very low concentrations of atractyloside (a plant glycoside) or bongkrekic acid (an antibiotic from a mold). Atractyloside binds to the translocase when its nucleotide site faces the cytoplasm, whereas bongkrekic acid binds when this site faces the mitochondrial matrix. Oxidative phosphorylation stops soon after either inhibitor is added, showing that ATP-ADP translocase is essential for maintaining adequate amounts of ADP to accept the energy associated with the proton-motive force.

b. Oligomycin-



Oligomycin, an antibiotic used as an antifungal agent, and dicyclohexylcarbodiimide (DCC) prevent the influx of protons through ATP synthase by binding to the carboxylate group of the c subunits required for proton binding. Modification of only one c subunit by DCC is sufficient to inhibit the rotation of the entire c ring and hence ATP synthesis. If actively respiring mitochondria are exposed to an inhibitor of ATP synthase, the electron-transport chain ceases to operate. This observation clearly illustrates that electron transport and ATP synthesis are normally tightly coupled.

c. Rotenone-

Rotenone, which is used as a fish and insect poison, and amytal, a barbiturate sedative, block electron transfer in NADH-Q oxidoreductase and thereby prevent the utilization of NADH as a substrate. Rotenone, as an electron-transport-chain inhibitor, may play a role, along with genetic susceptibility, in the development of Parkinson disease. In the presence of rotenone and amytal, electron flow resulting from the oxidation of succinate is unimpaired, because these electrons enter through QH_2, beyond the block. Antimycin A interferes with electron flow from cytochrome b in Q-cytochrome c oxidoreductase. Furthermore, electron flow in cytochrome

c oxidase can be blocked by cyanide , azide , and carbon monoxide (CO).

d. Cyanide- Cyanide and azide react with the ferric form of heme a_3, whereas carbon monoxide inhibits the ferrous form. Inhibition of the electron-transport chain also inhibits ATP synthesis because the proton-motive force can no longer be generated.

25. d) Decrease proton gradient

a. Lower BMR-This does not happen with 2,4 dinitrophenol

b. Raise R,Q- This does not happen with 2,4 dinitrophenol

c. Lower R.Q -This does not happen with 2,4 dinitrophenol

d. Decrease proton gradient

The tight coupling of electron transport and phosphorylation in mitochondria can be uncoupled by 2,4-dinitrophenol (DNP) and certain other acidic aromatic compounds. These substances carry protons across the inner mitochondrial membrane. In the presence of these uncouplers, electron transport from NADH to O_2 proceeds in a normal fashion, but ATP is not formed by mitochondrial ATP synthase, because the proton motive force across the inner mitochondrial membrane is continuously dissipated. This loss of respiratory control leads to increased oxygen consumption and oxidation of NADH. Indeed, in the accidental ingestion of uncouplers, large amounts of metabolic fuels are consumed, but no energy is captured as ATP. Rather, energy is released as heat. DNP is the active ingredient in some herbicides and fungicides. Remarkably, some people consume DNP as a weight-loss drug, despite the fact that the FDA banned its use in 1938. There are also reports that Soviet soldiers were given DNP to keep them warm during the long Russian winters. Chemical uncouplers are nonphysiological, unregulated counterparts of uncoupling proteins.

26. c) Inhibition of ATP synthesis with normal electron transport

[Ref: Stryer 8th Edition]

a. Inhibtion of cytochrome b- dinitrophenol is not an inihibitor of ETC.

b. Blockade of both electron transport and ATP synthesis- dinitrophenol is not an inihibitor of ETC and not of ATP synthesis.

c. Inhibtion of ATP synthesis with normal electron transport –

The tight coupling of electron transport and phosphorylation in mitochondria can be uncoupled by 2,4-dinitrophenol (DNP) and certain other acidic aromatic compounds. These substances carry protons across the inner mitochondrial membrane. In the presence of these uncouplers, electron transport from NADH to O_2 proceeds in a normal fashion, but ATP is not formed by mitochondrial ATP synthase, because the proton motive force across the inner mitochondrial membrane is continuously dissipated. This loss of respiratory control leads to increased oxygen consumption and oxidation of NADH. Indeed, in the accidental ingestion of uncouplers, large amounts of metabolic fuels are consumed, but no energy is captured as ATP. Rather, energy is released as heat. DNP is the active ingredient in some herbicides and fungicides. Remarkably, some people consume DNP as a weight-loss drug, despite the fact that the FDA banned its use in 1938. There are also reports that Soviet soldiers were given DNP to keep them warm during the long Russian winters. Chemical uncouplers are nonphysiological, unregulated counterparts of uncoupling proteins.

d. Inhibition of electron transport but not ATP synthesis - dinitrophenol is not an inihibitor of ETC.

27. b) Cu

[Ref: Harper 30th Edition]

a. Ca++ -Is not a part of Cytochrome oxidase

b. Cu-

Molecular Oxygen Is Reduced to Water via Complex IV Reduced cytochrome c is oxidized by Complex IV (cytochrome c oxidase), with the concomitant reduction of O2 to two molecules of water:

$$4\text{Cyt}\,c_{\text{reduced}} + O_2 + 8H^+_{\text{matrix}} \rightarrow 4\text{Cyt}\,c_{\text{oxidized}} + 2H_2O + 4H^+_{\text{intermembrane space}}$$

This transfer of four electrons from cytochrome c to O2 involves two heme groups, a and a3, and Cu . Electrons are passed initially to a Cu center (CuA), which contains 2Cu atoms linked to two protein cysteine-SH groups (resembling an Fe-S), then in sequence to heme a, heme a3, a second Cu center, CuB, which is linked to heme a3, and finally to O2. Of the eight H+ removed from the matrix, four are used to form two water molecules and four are pumped into the intermembrane space. Thus, for every pair of electrons passing down the chain from NADH or FADH2, 2H+ are pumped across the membrane by Complex IV. The O2 remains tightly bound to Complex IV until it is fully reduced, and this minimizes the release of potentially damaging intermediates such as superoxide anions or peroxide which are formed when O2 accepts one or two electrons, respectively.

c. Mn - Is not a part of Cytochrome oxidase

d. Zn - Is not a part of Cytochrome oxidase

28. b) Malonate

a. Cyanide -

Cyanide can be lethal because it binds to the ferric form of cytochrome oxidase and thereby inhibits oxidative phosphorylation. Nitrite converts ferrohemoglobin into ferrihemoglobin, which also binds cyanide. Thus, ferrihemoglobin competes with cytochrome c oxidase for cyanide. This competition is therapeutically effective because the amount of ferrihemoglobin that can be formed without impairing oxygen transport is much greater than the amount of cytochrome c oxidase.

b. Malonate- Malonate is a competitive inhibitor of Complex II.

c. H2S - The classic poisons H_2S, carbon monoxide, and cyanide inhibit Complex IV and can therefore totally arrest respiration.

d. CO - The classic poisons H2S, carbon monoxide, and cyanide inhibit Complex IV and can therefore totally arrest respiration.

29. c) 1.5

a. 1

b. 2.5

c. 1.5 - the electron-transport chain oxidizes the NADH and $FADH_2$ formed in the citric acid cycle. The transfer of electrons from these carriers to O_2, the ultimate electron acceptor, leads to the generation of a proton gradient across the inner mitochondrial membrane. This proton-motive force then powers the generation of ATP; the net stoichiometry is about 2.5 ATP per NADH, and 1.5 ATP per $FADH_2$.

d. 2

30. c) NAD+

a. Acetyl-CoA Production -this is not a part of ETC.

b. Aconitase-this is not a part of ETC

c. NAD+-cyanide blocks ETC.NAD+ Is part of ETC.

d. Citrate- this is not a part of ETC.

Molecular Biology – Questions

Q1. Klenow fragment lacks the activity of?

a. 3′-5′ exonuclease
b. 5′-3′ exonuclease
c. 5′-3′ DNA polymerase
d. 3′-5′ DNA polymerase

Q2. Which of the following techniques is based on RNA?

a. RT PCR
b. Sanger's technique
c. Next generation sequencing
d. Western blot

Q3. Which of the following does not require 5′ capping?

a. tRNA of alanine
b. U6 snRNA
c. mRNA for histone
d. siRNA

Q4. Which of the following does not favour permissive euchromatin due to changes occurring at cytosine residues at CpG islands in DNA?

a. Methylation
b. Phosphorylation
c. Alkylation
d. Sumoylation

Q5. During DNA replication which bond breaks:

a. Phosphodiester bonds
b. Phosphate bond
c. Hydrogen bond
d. Glycosidic bonds

Q6. Which RNA contains abnormal purine and pyrimidine:

a. tRNA
b. 23SrRNA
c. 16SrRNA
d. 5SrRNA
e. mRNA

Q7. Component of 50S ribosomal subunit:

a. 16S RNA
b. 18S RNA
c. 5.8 RNA
d. 5S RNA
e. 23S RNA

Q8. True about Chromatin remodelling:

a. Energy is required to displace the histone octamers from DNA or translocate them onto neighboring DNA segments
b. Histone modifications by specific enzyme
c. Do not involve enzymes
d. Aberrations in chromatin remodeling proteins may be associated with cancer

Q9. Best assessment of protein binding regions on a DNA molecule can be done by:

a. DNA foot-printing
b. RT PCR
c. Microarray
d. Western blotting
e. Northern blotting

Q10. Hyperuricemia is/are associated with:

a. HGPRT deficiency
b. HGPRT overactivity
c. PRPP synthetase deficiency
d. Glucose 6-phophatase deficiency
e. Glucose phosphate dehydrogenase deficiency

Q11. DNA microarrays allow detection of gene mutations using?

a. Polymerase chain Reaction
b. Cloning
c. Southern Blotting
d. Hybridization

Q12. True regarding cytoplasmic mRNA?

a. It is chiefly translated from nuclear DNA
b. The sugar is deoxyribose
c. Thymine is present in place of uracil
d. Its MW is greater than heterogenous RNA

1. b	2. a	3. a	4. a	5. c	6. a	7. d, e	8. a, b, d	9. a	10. a, d
11. d	12. b								

Q13. True statement regarding base excision repair is?

a. Used only for the bases which are deaminated
b. Uses enzyme called as DNA glycosylase which generate abasic sugar site
c. Removes about 10 – 15 nucleotide
d. Recognizes a bulk lesion

Q14. Fluoroquinolones (ciprofloxacin) act by inhibiting bacterial DNA gyrase. What is the function of DNA gyrase?

a. Unwind the DNA
b. Relieve torsional strain on DNA
c. Initiation of transcription
d. Synthesis of Okazaki Fragments

Q15. Membrane proteins are synthesized in

a. Free ribosome
b. Bound ribosome
c. Nucleolus
d. Mitochondria

Q16. All but one of the following histones are found located within the superhelix formed between DNA and the histone octamer; this histone is?

a. Histone H2B
b. Histone H3
c. Histone H1
d. Histone H3

Q17. Which of the following histone amino acids are typically acetylated?

a. Lysine
b. Arginine
c. Histidine
d. Leucine

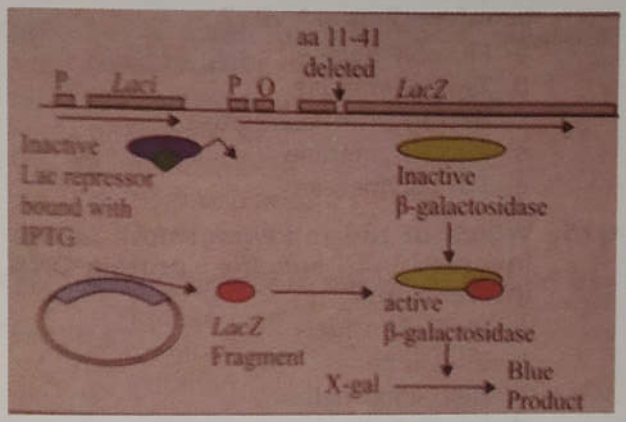
Q18. Which sequences extend between the 5' methyl-guanosine cap present on eukaryotic mRNAs to the AUG initiation codon?

a. Last exon
b. Last intron
c. 3' UTR
d. 5' UTR

Q19. Aminoacyl –tRNA synthetases must be capable of recognizing which of the following?

a. A specific tRNA and a specific amino acid
b. A specific tRNA and the 40S ribosomal subunit
c. A specific amino acid and the 40S ribosomal subunit
d. A specific amino acid and the 60S ribosomal subunit

Q20. Identify the phenomenon shown below?



a. Translation
b. Transformation
c. Complementation
d. Conjugation

Q21. Best investigation for metabolic disorder is?

a. Western blot
b. Tandem mass spectrometry
c. PCR
d. Gel electrophoresis

Q22. Restriction Fragment Length Polymorphism (RFLP) was used in-order to identify the five different spices of staphylococci in a surgical ICU. Which of the following site does the restriction enzyme act?

a. TAGATA- ATCTAT
b. ATGGAC – TACGTG
c. AATATA – TATAAT
d. GATATC – CTATAG

Q23. During the process of protein synthesis, the factor eEF-2 induces the hydrolysis of GTP. The energy of this hydrolysis is coupled to which of the following?

a. Amino acid activation by attachment to a tRNA
b. Correct alignment of the mRNA on the 40S ribosome
c. Formation of the 80S initiation complex
d. Translocation of the ribosome

13. b	14. b	15. b	16. c	17. a	18. d	19. a	20. c	21. b	22. d
23. d									

Q24. Which of the following DNA polymerase used in PCR has proofreading activity?

a. Pfu polymerase
b. Taq polymerase
c. Bestaq DNA Polymerase
d. Pwo Polymerase
e. Tth polymerase

Q25. Which of the following motif is/are involved in specific protein-DNA interactions?

a. Helix-turn-helix
b. Zinc finger
c. Helix-loop-helix
d. Leucine zipper

Q26. Which of the following protein (s) is/are required for DNA strand separation?

a. DNA Helicase
b. Single-stranded DNA-binding (SSB) proteins
c. Ligase
d. DNA polymerase
e. DnaA protein

Q27. Component (s) involved in RNA-induced silencing complex (RISC):

a. miRNa
b. Drosha
c. Dicer
d. Pasha
e. Slicer

Q28. In which of the following autosomal non-disjunction is/are seen:

a. Patau syndrome
b. Edward syndrome
c. Klinefelter syndrome
d. Cri-du-chat syndrome
e. William syndrome

Q29. Microsatellite instability disorder (s) is/are:

a. Myotonic dystrophy
b. Huntington chorea
c. Ataxia telangiectasia
d. Spinocerebellar ataxia
e. Xeroderma pigmentosa

Q30. Which of the following is/are part of 30S initiation complex:

a. ATP
b. GTP
c. Initiation factor
d. Elongation factor
e. mRNA

Q31. Single mutation in DNA of somatic cell of multicellular organism results in:

a. No effect on organism
b. Every cell in the entire organism will be affected
c. May result in 100 abnormal cells
d. Can be transmitted to progeny

Q32. A 5-years-old boy presents with mental retardation and self-mutilation behaviour. His serum uric acid levels are increased. The most probable enzyme deficient in this boy is:

a. Xanthine oxidase
b. HGPRT transferase
c. PRPP synthetase
d. Orotic acid dehydrogenase

Q33. Fluorescence in situ hybridization is done:

a. To identify specific DNA sequences
b. To map the location of mutant genes
c. To identify cistrons
d. To locate the site of replication

Q34. Nucleotide repeat in telomere results in:

a. Decreased cell division
b. Increased cell division
c. Formation of SNP
d. Addition of poly – A tail

Q35. Melting temperature of DNA is:

a. Directly proportional to GC pairing
b. Not relate to base pair compositions
c. Proportional to AT pairing
d. Proportional to length of DNA

Q36. Function of pseudouridine arm of tRNA:

a. It identifies amino acyl t-RNA synthetase and attaches to t-RNA
b. It identifies correct amino acid and attaches to t-RNA
c. For t-RNA ribosomal binding
d. Identifies m-RNA and attaches to it

24. a, c, d	25. a, b, d	26. a, b, e	27. a, c, e	28. a, b	29. a, b, d	30. b, c, e
31. c	32. b	33. b	34. b	35. a	36. c	

Q37. Rate limiting step in de novo purine synthesis:

a. PRPP glutamine amidotransferase
b. PRPP synthase
c. IMP dehydrogenase
d. Carbomyl phosphate synthatase-2

Q38. The best method to identify single nucleotide polymorphism (SNP) without a prior sequence information is:

a. DNA microassay
b. DNA sequencing
c. PCR
d. Fusion gene microassay

Q39. Which of the following test is used to identify mRNA?

a. Northern blot
b. Western blot
c. Southern blot
d. South-western blot

Q40. RNA is present in

a. Cytoplasm b. Nucleus
c. Ribosome d. All of the above

Q41. Adenosine deaminase deficiency is seen in

a. Severe combined immunodeficiency
b. Wiskot Aldrich syndrome
c. Agammaglobulinemia
d. None of the above

Q42. Epigenetics is not due to gene mutation. It is detected by

a. Bisulphite sequence
b. HPLC
c. Methylation
d. ChIP on chip

Q43. DNA finger printing is done by

a. Splitting DNA
b. DNA of WBC
c. DNA from nucleated cells
d. All of the above

Q44. Gene is?

a. Codon b. Anticodon
c. Cistron d. Okazaki fragment

Q45. Splicing activity is a function of

a. mRNA b. snRNA
c. rRNA d. tRNA

Q46. In leucine zipper model, leucine residue after every-

a. 3 amino acids
b. 6 amino acids
c. 9 amino acids
d. 12 amino acids
e. 7 amino acid

Q47. Gene transfer in bacterial system by

a. Transformation b. Transduction
c. Conjugation d. Location
e. Mutation

Q48. Translocation is necessary for

a. Initiation of codon
b. Binding of mRNA to ribosomes
c. Finding of proteins
d. Elongation of proteins

Q49. Cation used in PCR is

a. Calcium b. Lithium
c. Magnesium d. Sodium

Q50. Radiasensitive stage of cell cycle

a. G2 b. M
c. S d. G1

Radio sensitive is M Phase.

Q51. tRNA met would recognize

a. AUG b. UGC
c. GUG d. GCU

Q52. Western Blot detects?

a. DNA b. RNA
c. Protein d. mRNA

Q53. Which of following techniques is used for detection of variations in DNA sequence and Gene expression?

a. Northern blot b. Southern blot
c. Western blot d. Microarray

Q54. PCR detects

a. Antigen b. Antibody
c. Nucleic acid d. All of above

Q55. Mitochondrial DNA is

a. Paternally inherited
b. Maternally transmitted
c. Horizontal inheritance
d. Vertical inheritance

37. a	38. b	39. a	40. d	41. a	42. d	43. d	44. c	45. b	46. e
47. a	48. d	49. c	50. b	51. a	52. c	53. d	54. c	55. b	

Q56. Ladder pattern of DNA electrophoresis in apoptosis is caused by the action of the following enzyme

a. Endonuclease b. Transglutaminase
c. DNA se d. Caspase

Q57. Y chromosome is

a. Metacentric
b. Submetacentric
c. Acrocentric
d. Longer than the X chromosome

Q58. Known genetic loci are determined by

a. RT-PCR
b. Karyotyping
c. FISH
d. Chromosomal painting

Q59. Coding portion of DNA is .....of total chromosomal DNA

a. 1% b. 0.02%
c. 2% d. 20%

Q60. Chargaff rule states that

a. A+G = T+C
b. A/T = G/C
c. A = U = T = G = CT
d. A+T = G+C

Q61. Thymidine is a

a. Base b. Nucleoside
c. Nucleotide d. None of the above

Q62. In DNA structure, maximum number of bonds is seen amongst which of the following pair

a. A-T b. G-C
c. A-G d. C-T

Q63. DNA double helix is maintained by

a. Hydrogen bond
b. Vanderwaal forces
c. Disulfide linkage
d. Covalent bond

Q64. RNA does not contain

a. Uracil
b. Phosphate
c. Ribose
d. Dehydroxy-methyltaurine

Q65. The scientist who described structure of DNA is

a. Khorana
b. Watson & Crick
c. Subba Rao
d. None of the above

Q66. The Watson's Crick double helix model of DNA is

a. Right handed anti parallel
b. Left handed anti parallel
c. Right handed parallel
d. Left handed parallel

Q67. High energy compound is

a. ADP
b. ATP
c. Glucose-6-phosphate
d. AMP

Q68. Substrate for ATP synthase is

a. AMP b. ADP
c. IMP d. GMP

Q69. Which of the following is not a pyrimidine base?

a. Cytosine b. Uracil
c. Guanine d. Thymine

Q70. In Spectroscopy, necleotides absorb at 260 mm. This absorbance is due to

a. Purines and Pyrimidines
b. Deoxribose
c. Ribose
d. Histone
e. Phosphate

Q71. Transversion is seen in

a. Guanine-cytosine
b. Guanine-adenine
c. Guanine-thymine
d. Adenine-thymine
e. Cytosine-thymine

Q72. DNA fingerprinting was founded by

a. Wastson b. Galton
c. Jeffrey d. None

Q73. Components of 60S subunit of ribosome are

a. 5.8 S b. 23 S
c. 16 S d. 18 S
e. 28 S

56. a	57. c	58. c	59. b	60. a	61. b	62. b	63. a	64. d	65. b
66. a	67. b	68. b	69. c	70. a	71. a, c, d	72. c	73. a, e		

Q74. Proteins presents in Deoxyribonucleic acid is

a. Protamines b. Histone
c. Albumins d. Globulins

Q75. What is involved in formation of d-TMP from d-UMP?

a. N 5, N 10-methylene tetrahydrofolate
b. Form imino folate
c. N5 formyl folate
d. Dihydro folate

Q76. True about nucleosome

a. Use only one type of histone protein
b. Each complex is separated form each other by non histone protein
c. Regular repeating structure of DNA & histone proteins
d. Reflect small nucleus

Q77. DNA melting refers to:

a. Splitting of DNA into single strands
b. Breaking DNA into fragment
c. Breaking DNA down to bases
d. Fusion of DNA

Q78. PCR is used to -

a. Seal sticky ends
b. Cleave bacterial plasmids
c. Create artificial plasmids
d. Amplify a small amount of DNA

Q79. True about genetic code except :

a. Degenerate b. Overlapping
c. Ambiguous d. Universal
e. Commaless

Q80. True about mitochondrial DNA

a. UGA codes for tryptophan
b. Codes for 13 protein
c. High content of untranslated sequence
d. Circular double stranded DNA
e. Mitochondrial disease occur due to point mutation and large scale rearrangements .

Q81. Which of the following enzymes is DNA dependent RNA polymerase :

a. DNA ligase
b. Primase
c. DNA polymerase III
d. RNA transcriptase

Q82. Frameshift mutation leads to cellular changes to which of the following processes

a. Transcription b. Translation
c. Replication d. Spontaneous

Q83. In Pyrimidine synthesis rate limiting enzyme is *

a. Dihydroorotase dehydrogenase
b. Carbamoyl phosphate synthetase II
c. Aspartate transcarbomylase
d. OMP. Decarboxylase

Q84. Which of the following compound is an analogue of hypoxanthine :

a. Arabinoside C
b. Allopurinol
c. Ribose phosphate
d. 5-phosphoribosylpyrophophate (PRPP)

Q85. Which of the following statement describing restriction endonucleases is true:

a. They always yield overhanging single-stranded ends
b. They recognize methylated DNA sequences
c. The recognize triplet repeats
d. They cleave both strands in duplex DNA

Q86. True about gene library:

a. Also known as chromosome
b. Library that contains books on gene
c. Computer base with all gene knowledge
d. DNA nucleotide or fragment
e. Complete collection of gene copies of one organism

Q87. After digestion by restriction endonucleases DNA strands can be joined again by:

a. DNA polymerase
b. DNA ligase
c. DNA topiosomerase
d. DNA gyrase

74. b	75. a	76. c	77. a	78. d	79. b, c, d	80. a, b, d, e	81. b
82. b	83. b, c	84. b	85. d	86. e	87. b		

Q88. True about sickle disease are all, except:

a. Single nucleotide change results in change of Glutamine to Valine
b. Sticky patch is generated as a result of replacement of a non polar residue with a polar residue
c. HbS confers resistance against malaria in heterozygotes
d. RFLP results from a single base change

Q89. Xeroderma pigmentosa is caused due to a group of closely related abnormalities in :

a. Mismatch repair
b. Base excision repair
c. Nucleotide excision repair
d. SOS repair

Molecular Biology – Explanations

1. b) 5'-3' exonuclease

Klenow fragment is a large protein fragment produced when DNA polymerase I from E. coli is enzymatically cleaved by the protease subtilisin.

Large (Klenow) fragment of DNA polymerase I. This polymerase is widely distributed in bacteria. The Klenow fragment, produced by proteolytic treatment of the polymerase, retains the polymerization and proofreading activities of the enzyme. The Klenow fragment shown here is from the thermophilic bacterium. The active site for addition of nucleotides is deep in the crevice at the far end of the bound DNA. The dark blue strand is the template.

2. a) RT PCR

[Ref: Harper's Illustrated biochemistry, 30th Edition]

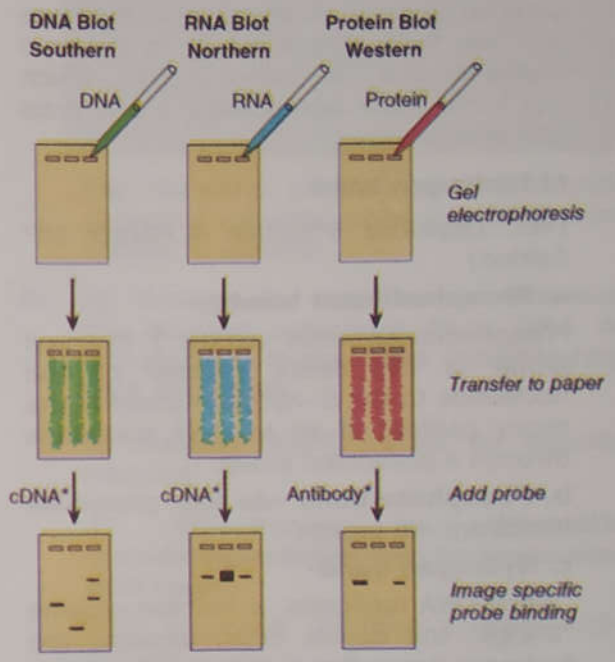
a. RT PCR-A method used to quantitate mRNA levels that rely upon a first step of cDNA copying of mRNAs catalysed by reverse transcriptase prior to PCR amplification and quantitation.

b. Sanger's technique- Frederick Sanger reduced the disulphide bonds, separated the A and B chains, and cleaved each chain into smaller peptides using trypsin, chymotrypsin, and pepsin. The resulting peptides were then isolated and hydrolysed into a mixture of smaller peptides by treatment with acid. Each peptide in the mixture was isolated and treated with 1-fluoro-2,4-dinitrobenene (Sanger reagent), which reacts with the exposed a-amino groups of the amino-terminal residues. The amino acid content of each peptide was then determined and the amino-terminal amino acid identified.

c. Next generation sequencing-Modified methods of genome sequencing. It has significantly reduced the cost and time taken for whole genome sequencing. It is a technique similar to Sanger sequencing, done on DNA.

d. Western blot

A method for transferring protein to a nitrocellulose filter, on which the protein can be detected by a suitable probe (e.g., an antibody).



3. a) tRNA of alanine

[Ref: Harper's Illustrated biochemistry, 30th Edition]

- Small nuclear RNAs contain unique 5'-caps. Sm-class snRNAs are found with 5'-trimethylguanosine caps, while Lsm-class snRNAs are found with 5'-monomethylophosphate caps.
- mRNAs do have a 7-methylguanylate cap, abbreviated m7G.
- tRNAs and rRNAs don't require 5' Capping. The have other modifications.

4. a) Methylation

[Ref: Harper's Illustrated biochemistry, 30th Edition]

The CpG sites or CG sites are regions of DNA where a cytosine nucleotide is followed by a guanine nucleotide in the linear sequence

of bases along its 5′ → 3′ direction. CpG is shorthand for 5′-C-phosphate-G-3′. That is, cytosine and guanine separated by only one phosphate group; phosphate links any tow nucleosides together in DNA. The CpG notation is used to distinguish this single-stranded linear sequence from the CG base-pairing of cytosine and guanine for double-stranded sequences. CpG islands (or CG islands) are regions with a high frequency of CpG sites. Methylation of CpG sites in the promoter of a gene may inhibit gene expression. There is also evidence that low folate status results in impaired methylation of CpG islands in DNA, which is a factor in the development of colorectal and other cancers.

5. c) Hydrogen bond

[Ref: Lippincott 6thEdition & Harper 30th Edition]

a. Phosphodiester bonds –

Phosphodiester bonds join the 3′-hydroxyl group of the deoxy pentose of one nucleotide to the 5′-hydroxyl group of the deoxy pentose of an adjacent nucleotide through a phosphate group.

b. Phosphate bond –as such phosphate bonds are not broken

c. Hydrogen bond-

"When DNA replicates, a helicase enzyme "unzips" the double helix, breaking the hydrogen bonds that hold it together in the center" -www.boundless.com/physics

"Separation of the two DNA strands in the double helix: The two strands of the double helix separate when hydrogen bonds between the paired bases are disrupted. Disruption can occur in the laboratory if the pH of the DNA solution is altered so that the nucleotide bases ionize, or if the solution is heated. [Note: Phosphodiester bonds are not broken by such treatment]. Separation of the two strands over short regions occurs during both DNA and RNA synthesis" - Lippincott 6th/397-98

d. Glycosidic bonds -

In DNA, refers to the nitrogen-carbon linkage between the 9′ nitrogen of purine bases or 1′ nitrogen of pyrimidine bases and the 1′ carbon of the sugar group.

Add a note on:

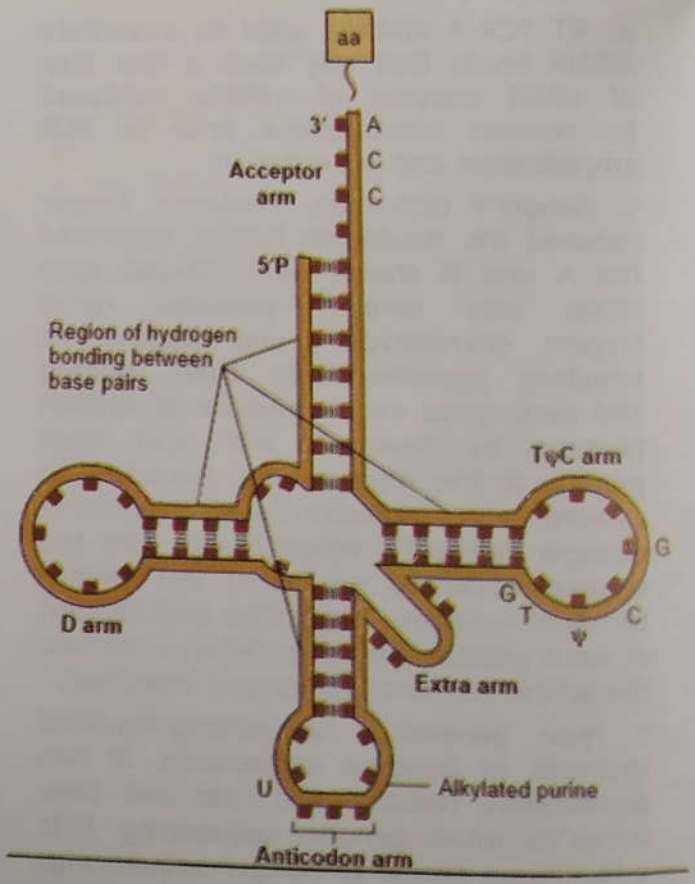
Protein	Function
DNA Polymerases	Deoxynucleotide polymerization
Helicases	Processive unwinding of DNA
Topoisomerases	Relieve torsional strain that results from helicase-induced unwinding
DNA primase	Initiates synthesis of RNA primers
Single-Strand binding proteins	Prevent premature reannealing of dsDNA
DNA ligase	Seals the single strand nick between the nascent chain and Okazaki fragments on lagging strand

6. a) tRNA

[Ref: Lippincott 6thEdition & Harper 30th Edition]

a. tRNA- "tRNA molecule contain a high percentage of unusual bases, for example, dihydrouracil and have extensive intra-chain base pairing that

leads to characteristic secondary and tertiary structure.



- tRNAs are the smallest (4S) of the three major types of RNA molecules. There is at least one specific type of tRNA molecule for each of the 20 amino acids commonly found in proteins. Together, tRNAs make up about 15% of the total RNA in the cell.
- The tRNA molecules contain a high percentage of unusual bases (for example, dihydro uracil) and have extensive intrachain base-pairing that leads to characteristic secondary and tertiary structure.

b. 23SrRNA-they do not have modified bases .

c. 16SrRNA-they do not have modified bases .

d. 5SrRNA-they do not have modified bases .

e. mRNA-they do not have modified bases.

7. d) 5S RNA
e) 23S RNA

[Ref: Lippincott's illustrated reviews, 6th Edition]

a. 16S RNA-It is part of 30S Prokaryotic subunit.

b. 18S RNA- It is part of 40S Eukaryotic subunit.

c. 5.8 RNA- It is part of 60S Eukaryotic subunit.

d. 5S RNA- It is part of 50S Prokaryotic subunit.

e. 23S RNA- It is part of 50S Prokaryotic subunit.

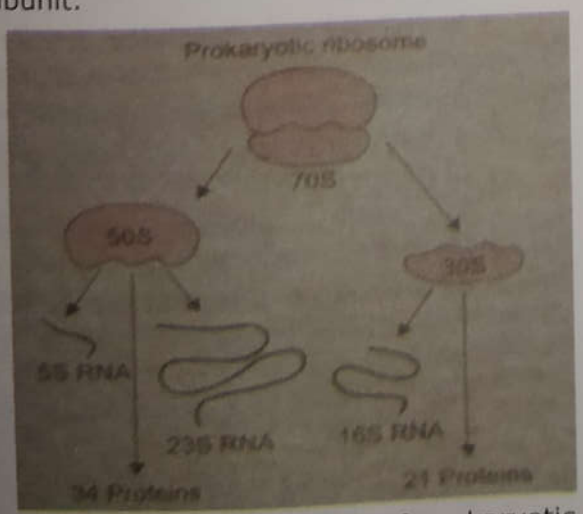


Fig: ribosomal composition of prokaryotic ribosome

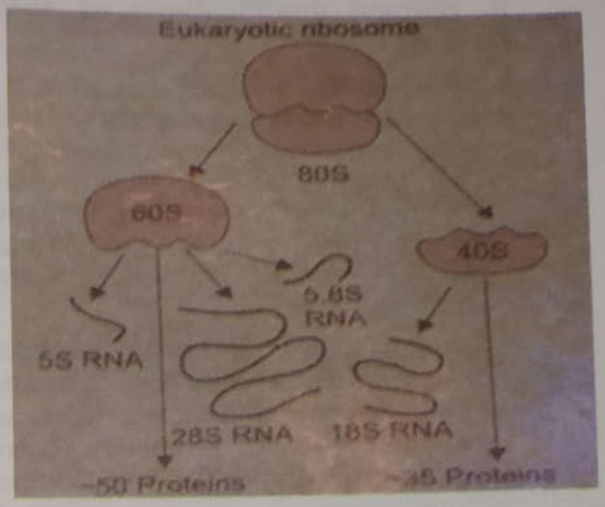


Fig: ribosomal composition of eukaryotic ribosomal subunits varies somewhat from species to species).

8. a) Energy is required to displace the histone octamers from DNA or translocate them onto neighboring DNA segments

b) Histone modifications by specific enzyme

d) Aberrations in chromatin remodeling proteins may be associated with cancer

[Ref: Lippincott 6thEdition & Harper 30th Edition]

a. Energy is required to displace the histone octamers from DNA or translocate them onto neighboring DNA segments –

- Histone covalent modification is an important determinant of gene activity. Histones are subjected to a wide range of specific post-translational modifications. These modifications are dynamic and reversible. Histone acetylation and deacetylation are best understood.
- The surprising discovery that histone acelylase and other enzymatic activities are associated with the coregulators involved in regulation of gene transcription.
- Together then coregulators (chromatin modifiers and chromatin remodellers), working in conjunction, can open up gene promoters and regulatory regions, facilitating binding of other trans factors and RNA polymerase II and GTFs.

b. Histone modifications by specific enzyme –

Chromatin Remodelers

- In general, two major mechanisms exist which regulate chromatin accessibility: First, histones can be post-translationally modified enabling the recruitment of specific effect or proteins to chromatin, thereby changing the activity state of chromatin domains.
- Second, specific chromatin remodeling complexes displace the histone octamers from DNA or translocate them onto neighboring DNA segments, thereby exposing underlying DNA sequences to sequence specific regulatory factors. The ATP-dependent chromatin remodeling enzymes are highly abundant in the cell, with about one remodeling complex per 10 nucleosomes and also and remarkably diverse.

c. Do not involve enzymes –it involves enzyme.

d. Aberrations in chromatin remodeling proteins may be associated with cancer-

- Chromatin remodeling is the dynamic modification of chromatin architecture to allow access of condensed genomic DNA to the regulatory transcription machinery proteins, and thereby control gene expression.
- Such remodeling is principally carried out by

1) Covalent histone modifications by specific enzymes, e.g., histone acetyltransferases (HATS), deacetylases, methyltransferases, and kinases, and

2) ATP-dependent chromatin remodeling complexes which either move, eject or restructure nucleosomes.

9. a) DNA foot-printing

[Ref: Lippincott 6thEdition & Harper 30th Edition]

a. DNA foot-printing –

- It is a molecular technique used to identify the specific DNA sequence (binding site) that binds to a protein.
- This technique mainly used to identify the transcription factors which bind to promoter, enhancer or silencer region of gene to regulate its expression. Therefore the regulation of transcription of a gene can be studied using this method.

b. RT PCR - A method used to quantitate mRNA levels that relies upon a first step of cDNA copying of mRNAs catalyzed by reverse transcriptase prior to PCR amplification and quantitation.

c. Microarray –refer to table below

d. Western blotting -refer to table below

e. Northern blottin- refer to table below

Technique	Sample Analysed	Gel Used	Purpose
Southern blot	DNA	Yes	Detect DNA changes
Northern blot	RNA	Yes	Measures mRNA amounts and size
Western blot	Protein	Yes	Measures protein amounts
ASO	DN	No	Detects DNA mutations
Microarray	RNA or cDNA	No	Measures many mRNA levels at once

10. a) HGPRT deficiency
d) Glucose 6-phophatase deficiency

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. HGPRT deficiency-

HGPRT deficiency (as seen in Lesch-Nyhan syndrome): Increased production of purines

b. HGPRT over activity-deficiency and not over activity which results in gout.

c. PRPP synthetase deficiency-

↑ PRPP synthetase: Increased production of purines

↑ PRPP glutamylamidotransferase: Increased production of purines

d. Glucose 6-phophatase deficiency-

"Von Glerke's disease (Type 1 glycogen storage disease): Hyperuricemia occurs due to Glucose 6-phosphatase enzyme defect" –

Primary gout (overproduction of uric acid): Important metabolic defects (enzymes)

- Glucose 6-phosphatase deficiency : Purine overproduction
- Elevation of glutathione reductase

e. Glucose phosphate dehydrogenase deficiency-Is most common cause of Hemolytic anemia.

Add a note on:

Metabolic Disorders of Purine and Pyrimidine Metabolism

Defective Enzyme	Major Signs and Symptoms
Purine Metabolism	
Hypoxanthine-guanine phosphoribosyl transferase	Lesch-Nyhan syndrome. Uricemia, self-mutalation
PRPP synthase	Gout; gouty arthritis
Adenosine deaminase	Severely compromised immune system
Purine nucleoside phosphorylase	Autoimmune disorders; benign and opportunistic infections
Pyrimidine Metabolism	
Dihydropyrimidine dehydrogenase	Can develop toxicity to 5-fluorouracil, also a substrate for this dehydrogenase
Orotate phosphoribosyl transferase and orotidylic acid decarboxylase	Orotic acid aciduria type 1; megaloblastic anemia
Orotidylic acid decarboxylase	Orotic acid aciduria type 2

11. d) Hybridization

a. Polymerase chain Reaction –

An enzymatic method for the repeated copying (and thus amplification) of the two strands of DNA that make up a particular gene sequence.

b. Cloning-

A clone is a large population of identical molecules, bacteria, or cells that arise from a common ancestor. Molecular cloning allows for the production of a large number of identical DNA molecules, which can then be characterized or used for other purposes. This technique is based on the fact that chimeric or hybrid DNA molecules can be constructed in cloning vectors— typically bacterial plasmids, phages, or cosmids—which then continue to replicate in a host cell under their own control systems. In this way, the chimeric DNA is amplified.

c. Southern Blotting –

A method for transferring DNA from an agarose gel to nitrocellulose filter, on which the DNA can be detected by a suitable probe (eg, complementary DNA or RNA).

d. Hybridization-

A hybridization based method that uses chromatin immunoprecipitation (ChIP) techniques to map, genome-wide, the in vivo sites of binding of specific proteins within chromatin in living cells. Sequence binding is determined by annealing fluorescently labeled DNA samples to microarrays (array).

12. a) It is chiefly translated from nuclear DNA

a. It is chiefly translated from nuclear DNA-RNA is synthesized from a DNA template by an RNA polymerase.

b. The sugar is deoxyribose -

The sugar is Ribose.

c. Thymine is present in place of uracil-

Uracil is present in place of thymine.

d. Its MW is greater than heterogenous RNA-

- In mammalian cells, including cells of humans, the mRNA molecules present in the cytoplasm are not the RNA products immediately synthesized from the DNA template but must be formed by processing from the pre-mRNA before entering the cytoplasm.

13. b) Uses enzyme called as DNA glycosylase which generate abasic sugar site

a. Used only for the bases which are deaminated –

Deamination of cytosine to uracil

b. Uses enzyme called as DNA glycosylase which generate abasic sugar site –

DNA Damaging agents-

- Oxygen radicals Hydrolysis Alkylating agents

DNA lesions formed-

- Abasic sites
- Single strand breaks

- 8-oxoguanine lesions

c. Removes about 10 – 15 nucleotide –

This is seen in mismatch repair.

d. Recognizes a bulk lesion -

This is seen in mismatch repair.

14. b) Relieve torsional strain on DNA

a. Unwind the DNA- by DNA Helicase

b. Relieve torsional strain on DNA- Relieve torsional strain that results from helicase-induced unwinding.

- The bacterial topoisomerase II (often called DNA gyrase) is the target of several antibiotics that inhibit the prokaryotic enzyme much more than the eukaryotic one.
- Novobiocin blocks the binding of ATP to gyrase.
- Nalidixic acid and ciprofloxacin, in contrast, interfere with the breakage and rejoining of DNA chains.
- These two gyrase inhibitors are widely used to treat urinary tract and other infections including those due to Bacillus anthracis (anthrax).
- Camptothecin, an antitumor agent, inhibits human topoisomerase I by stabilizing the form of the enzyme covalently linked to DNA.

c. Initiation of transcription -by RNA Polymerase

d. Synthesis of Okazaki Fragments-by DNAP III

15. b) Bound ribosome

a. Free ribosome-

b. Bound ribosome-

Polyribosomes actively synthesizing proteins can exist as free particles in the cellular cytoplasm or may be attached to sheets of membranous cytoplasmic material referred to as endoplasmic reticulum. Attachment of the particulate polyribosomes to the endoplasmic reticulum is responsible for its "rough" appearance as seen by electron microscopy. The proteins synthesized by the attached polyribosomes are extruded into the cisternal space between the sheets of rough endoplasmic reticulum and are exported from there. Some of the protein products of the rough endoplasmic reticulum are packaged by the Golgi apparatus for eventual export. The polyribosomal particles free in the cytosol are responsible for the synthesis of proteins required for intracellular functions.

c. Nucleolus-All of the rRNA molecules except the 5S rRNA, which is independently transcribed, are processed from a single 45S precursor RNA molecule in the nucleolus .The highly methylated rRNA molecules are packaged in the nucleolus with the specific ribosomal proteins.

In mammalian cells, the three rRNA molecules (28S, 18S, 5.8S) are transcribed as part of a single large 45S precursor molecule. The precursor is subsequently processed in the nucleolus to provide these three RNA components for the ribosome subunits found in the cytoplasm. The rRNA genes are located in the nucleoli of mammalian cells.

d. Mitochondria-

Encodes 13 protein subunit of respiratory chain:

- Seven subunits of NADH dehydrogenase (complex I)
- Cytochrome b of complex III
- Three subunits of cytochrome oxidase (complex IV)
- Two subunits of ATP synthase

16. c) Histone H1

Histones are a small family of closely related basic proteins. H1 histones are the ones least tightly bound to chromatin and are, therefore, easily removed with a salt solution, after which chromatin becomes more soluble.

a. Histone H2B -This forms part of Histone Octamer And hence Nucleosome. The histones interact with each other in very specific ways. H3 and H4 form a tetramer containing two molecules of each (H3–H4)2, while H2A and H2B form dimers (H2A–H2B). Under physiologic conditions, these histone oligomers associate to form the histone octamer of the composition (H3–H4)2–(H2A–H2B)2.

The organizational unit of this soluble chromatin is the nucleosome. Nucleosomes contain four major types of histones: H2A, H2B, H3, and H4.

b. Histone H3-This forms part of Histone Octamer And hence Nucleosome.

c. Histone H1- The ~145 bp of DNA, consisting of 1.75 superhelical turns, are in contact with the histone octamer. The position of histone H1, when it is present, is indicated by the dashed outline at the bottom of the figure. Histone H1 interacts with DNA as it enters and exits the nucleosome.

d. Histone H3-This forms part of Histone Octamer.And hence Nucleosome.

17. a) Lysine

a. Lysine –

Lysine bears a positively charged ammonium group at neutral pH. The addition of an acetyl group generates an uncharged amide group. This change dramatically reduces the affinity of the tail for DNA and modestly decreases the affinity of the entire histone complex for DNA, loosening the histone complex from the DNA

b. Arginine-is found in histones.

c. Histidine- is not found in histones.

d. Leucine- is not found in histones.

18. d) 5' UTR

a. Last exon-Is towards 3' UTR

b. Last intron-3' UTR

c. 3' UTR-

The poly(A) "tail" at the 3′-hydroxyl terminal of mRNAs maintains the intracellular stability of the specific mRNA by preventing the attack of 3′-exonucleases and also facilitates translation .A few mRNAs, including those for some histones, do not contain a poly(A) tail. Both the mRNA "cap" and "poly(A) tail" are added posttranscriptionally by nontemplatedirected enzymes to mRNA precursor molecules (pre-mRNA). mRNA represents 2% to 5% of total eukaryotic cellular RNA.

d.5' UTR –

Eukaryotic mRNAs have unique chemical characteristics. The 5′ terminal of mRNA is "capped" by a 7-methylguanosine triphosphate that is linked to an adjacent 2′-O-methyl ribonucleoside at its 5′-hydroxyl through the three phosphates .

19. a) A specific tRNA and a specific amino acid

a. A specific tRNA and a specific amino acid-

tRNA molecules have extraordinarily similar functions and three-dimensional structures. The adapter function of the tRNA molecules requires the charging of each specific tRNA with its specific amino acid. Since there is no affinity of nucleic acids for specific functional groups of amino acids, this recognition must be carried out by a protein molecule capable of recognizing both a specific tRNA molecule and a specific amino acid. At least 20-specific enzymes are required for these specific recognition functions and for the proper attachment of the 20 amino acids to specific tRNA molecules. This energy requiring process of recognition and attachment (charging) proceeds in two steps and is catalyzed by one enzyme for each of the 20 amino acids. These enzymes are termed aminoacyltRNA synthetases. The specific aminoacyl-AMP–enzyme complex then recognizes a specific tRNA to which it attaches the aminoacyl moiety at the 3′-hydroxyl adenosyl terminal. The charging reactions have an error rate of less than 10−4 and so are quite accurate. The amino acid remains attached to its specific tRNA in an ester linkage until it is polymerized at a specific position in the fabrication of a polypeptide precursor of a protein molecule.

b. A specific tRNA and the 40S ribosomal subunit-

c. A specific amino acid and the 40S ribosomal subunit

d. A specific amino acid and the 60S ribosomal subunit

20. c) Complementation

[Ref: Harper's Illustrated biochemistry, 30th Edition]

This is schematic representation of the Blue-white assay, used to screen for recombinant vectors. The method is based on the principle of α-complementation of the β-galactosidase gene. So phenomenon is complementation.

β-galactosidase is a protein encoded by the lacZ gene of the lac operon, and it exists as a homotetramer in its active state. However, a mutant β-galactosidase derived from the M15 strain of E. coli has

its N-terminal residues 11-41 deleted and this mutant, the -peptide, is unable to form a tetramer and is inactive. This mutant form of protein however may return fully to its active tetrameric state in the presence of an N-terminal fragment of the protein, the α-peptide. The rescue of function of the mutant β-galactosidase by the α-peptide is called α-complementation.

21. b) Tandem mass spectrometry

[Ref: Tietz Textbook of clinical chemistry and molecular biology, 5th EDITION]

Biochemical Genetics Tests: Analytical Considerations:

In addition to clinical presentation and routine laboratory tests, the diagnosis of patients with inborn errors of metabolism relies on specific tests such as ion-exchange chromatography and liquid chromatography with tandem mass spectrometry (LC-MS/MS) for amino acid analysis, gas chromatography/mass spectrometry (GC/MS) for organic acid analysis, tandem mass spectrometry (MS/MS) with (LC-MS/MS) or without liquid chromatographic separation for acylcarnitine profiles, and LC-MS/MS or GC/MS for acylglycine profiles. The combination of these tests, with the use of different specimen types, is the key to biochemical confirmation of metabolic disorders, whose diagnosis is then definitively confirmed using DNA testing or enzyme / transporter assays.

22. d) GATATC – CTATAG

a. TAGATA- ATCTAT-this not a pallindromic sequence

b. ATGGAC – TACGTG- this not a pallindromic sequence

c. AATATA – TATAAT- this not a pallindromic sequence

d. GATATC – CTATAG-

Enzymes known as restriction endonucleases, cleave double-stranded DNA at sites specified by a sequence of four, six, or more base pairs called restriction sites. Which recognize pallindromic sequence.

23. d) Translocation of the ribosome

a. Amino acid activation by attachment to a Trna - does not require eEF-2

b. Correct alignment of the mRNA on the 40S ribosome - does not require eEF-2

c. Formation of the 80S initiation complex- does not require eEF-2

d. Translocation of the ribosome-

Elongation Is Also a Multistep, Accessory Factor - Facilitated Process

Elongation is a cyclic process on the ribosome in which one amino acid at a time is added to the nascent peptide chain. The peptide sequence is determined by the order of the codons in the mRNA. Elongation involves several steps catalyzed by proteins called elongation factors (EFs).

These steps are

(1) binding of aminoacyl-tRNA to the A site,

(2) peptide bond formation,

(3) translocation of the ribosome on the mRNA, and

(4) expulsion of the deacylated tRNA from the P- and E-sites.

Translocation

The now deacylated tRNA is attached by its anticodon to the P site at one end and by the open CCA tail to the E site on the large ribosomal subunit . At this point, elongation factor 2 (EF2) binds to and displaces the peptidyl tRNA from the A site to the P site. In turn, the deacylated tRNA is on the E site, from which it leaves the ribosome. The EF2-GTP complex is hydrolyzed to EF2-GDP, effectively moving the mRNA forward by one codon and leaving the A site open for occupancy by another ternary complex of amino acid tRNA–EF1A-GTP and another cycle of elongation.

24. a) Pfu polymerase
c) Bestaq DNA Polymerase
d) Pwo Polymerase

[Ref: Lippincott 6thEdition & Vasudevan 5th Edition]

a. Pfu polymerase-

Pfu polymerase from Pyrococcus furiosus is used when increased accuracy is desired because it possesses proofreading ability-unlike Taq polymerase.

b. Taq polymerase-

"Taq polymerase remains to be the most ubiquitously used polymerase for PCR. This enzyme has a high rate of dNTP

25.

incorporation but does not have any proof-reading activity. This means that Taq is prone to introducing base-pair errors during PCR amplification. If the PCR product is to be used for functional protein analysis, then this can be problematic"-www.sciencedirect.com

Alternative Polymerases and PCR Modifications

- Since the introduction of Taq polymerase, a variety of other thermostable polymerases from other thermostable polymerases from other thermophilic organisms have also been used in PCR.

c. Bestaq DNA Polymerase-

"Both Bestaq DNA Polymerase and Kodaq DNA Polymerase have excellent proofreading ability and processivity, with a processing speed of 3-4kb and 1kb per minute, respectively"-www.abmgood.com

KOD DNA polymerase is a recombinant form of DNA polymerase derived from the thermophilic solfatara bacterium. Thermococcus kodakaraensis KOD1 type strain. KOD DNA polymerase functions optimally at 85°C and displays 3'-5' exonuclease proofreading activity, producing blunt-ended DNA products-www.abmgood.com

d. Pwo Polymerase-

"Two DNA polymerase is derived from the ultra-thermophilic archaeon Pyrococcus woesei found in deep marine environments (24). Pwo polymerase funcitons optimally at 100-103°C, and displays high proofreading 3'-5' exonuclease activity, giving it 18-fold higher fidelity than Taq polymerase"-www.abmgood.com

e. Tth polymerase-

"Tth polymerase is derived from Thermus thermophiles, a thermophilic thermal vent bacterium (25). Tth DNA polymerase functions optimally at 75°C with high processivity, but lacks proofreading 3'-5' exonuclease activity"-www.abmgood.com

25. All

[Ref: Harper 30th Edition& Satyanarayan 4th Edition]

a. Helix-turn-helix

Binding Motif	Organism	Regulatory Protein
Helix-turn-helix	E coli Phage Mammals	Lac repressor, CAP cI, cro, and 434 repressors Homeobox proteins Pit-1, Oct1, Oct2

b. Zinc finger

Binding Motif	Organism	Regulatory Protein
Zinc finger	E coli Yeast Drosophila Xenopus Mammals	Gene 32 protein Gal4 Serenditpity, hunchback TFIIIA Steroid receptor family, Sp1

c. Helix-loop-helix

Motifs may be associated with particular functions. Proteins that bind to DNA contain a limited number of motifs. The helix-loop-helix motif is an example found in a number of proteins that function as transcription factors.

d. Leucine zipper

Binding Motif	Organism	Regulatory Protein
Leucine zipper	Yeast mammals	GCN4 C/EBP, fos, June, Fra-1, CRE binding protein (CREB), c-myc, n-myc, l-myc

26. a) DNA Helicase
b) Single-stranded DNA-binding (SSB) proteins
e) DnaA protein

[Ref: Harper 30th Edition & Lippincott 6th Edition & Satyanarayan 4th Edition]

a. DNA Helicase-

These enzymes bind to ssDNA near the replication fork, and then move into the neighboring double-stranded region, forcing the strands apart-in defect, unwinding the double helix. Helicases require energy provided by ATP [Note: DMD is the principal helicase of replication in E. coli. Its binding to DNA requires DnaC.]

b. Single-stranded DNA-binding (SSB) proteins-

These proteins bind to the ssDNA generated by helicases. They bind cooperatively-that is, the binding of one molecule of SSB protein makes it easier for additional molecules of SSB protein to bind tightly

to the DNA strand. The SSB proteins are not enzymes, but rather serve to shift the equilibrium between dsDNA and ssDNA in the direction of the single-stranded forms. These proteins not only keep the two stands of DNA separated in the area of the replication origin, thus providing the single-stranded template required by polymerases, but also protect the DNA from nucleases that degrade ssDNA.

c. Ligase

Enzyme	Reaction	Primary Use
DNA ligase	Catalyzes bonds between DNA molecules	Joining of DNA molecules

d. DNA polymerase

Enzyme	Reaction	Primary Use
DNA polymerase I	Synthesizes double-stranded DNA from single-stranded DNA	Synthesis of double-stranded cDNA; nick translation; generation of blunt ends from sticky ends

e. DnaA protein-

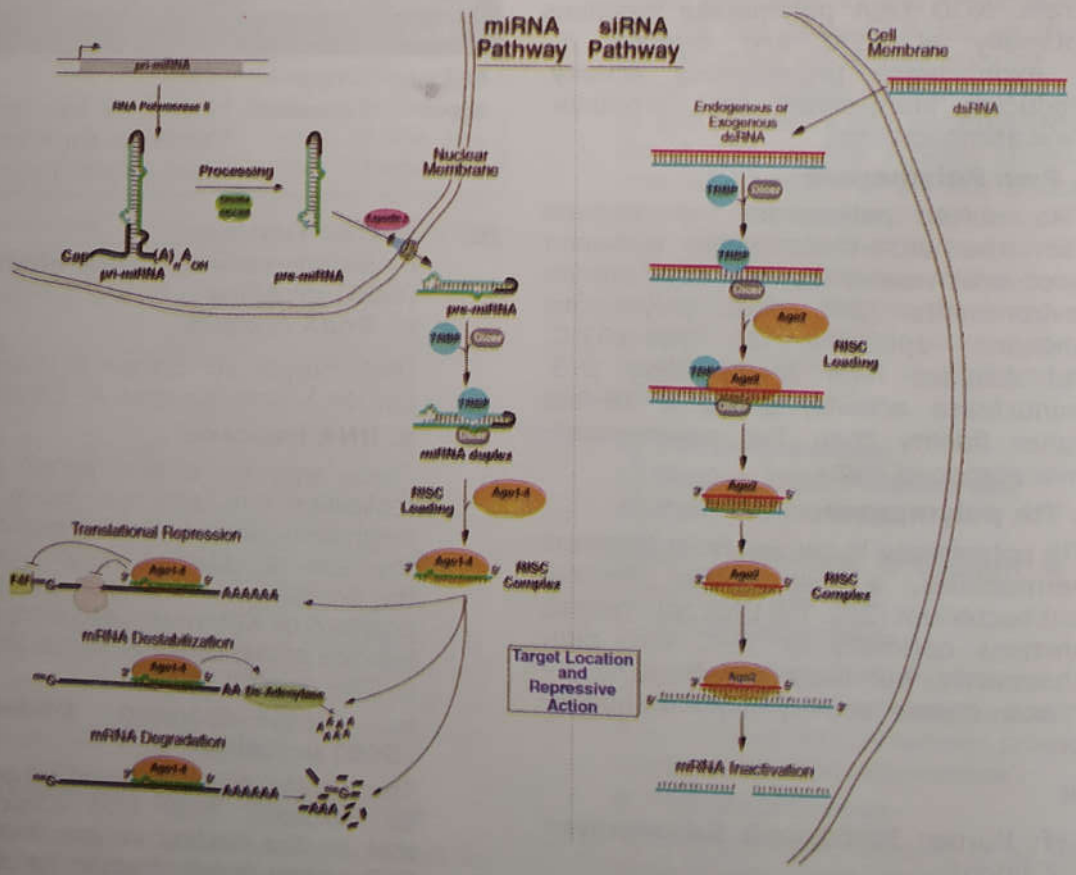
DnaA protein binds to specific nucleotide sequences at the origin of replication, causing short, tandemly arranged (one after the other) AT-rich regions in the origin to melt. Melting is ATP-dependent, and results in strand separation with the formation of localized regions of ssDNA.

27. a) miRNa
c) Dicer
e) Slicer

[Ref: Harper 30th Edition]

a. miRNa

miRNAs: MicroRNAs, 21 to 22 nucleotide long RNA species derived from RNA polymerase II transcription units, and 500 to 1500 bp in length via RNA processing. These RNAs play crucial roles in gene regulation by altering mRNA function.



b. Drosha-please see option a

c. Dicer- please see option a

d. Pasha

DGCR8/Pasha is an essential cofactor for Drosha, a nuclear RNase III that cleaves the local hairpin structures embedded in long primary microRNA transcripts (pri-miRNAs) in eukaryotes. DsRNA-binding proteins that contain dsRNA-binding domains (dsRBDs) serve diverse roles during RNA metabolism. A recently emerging theme in RNA silencing pathways is that multidomain RNase III proteins, such as Drosha and Dicer, necessitate dsRNA-binding proteins for miRNA processing and/or RISC formation. For example, Dcr-1 in Drosophila interacts with Loquacious/ R3DI that contains three dsRBDs and is required for miRNA processing, and possibly also for RISC assembly.

e. Slicer

28. a) Patau syndrome
b) Edward syndrome

[Ref: Robbins 9th Edition & Harrison 19th Edition]

a. Patau syndrome

b. Edward syndrome

c. Klinefelter syndrome

"Klinefelter syndrome: The classic form of KS (47, XXY) occurs after meiotic nondisjunction of the sex chromosomes during gametogenesis (40% during spermatogenesis, 60% during oogenesis)"-Harrison 19th/2350

d. Cri-du-chat syndrome

"The first chromosome deletion syndromes were diagnosed clinically and were subsequently demonstrated to be caused by a chromosome deletion on cytogenetic analysis. Examples of these disorders include the Wolf-Hirschhorn syndrome, which is associated with deletions of a small region of the short arm of chromosome 4 (4p); the cri-du-chat syndrome, associated with deletion of a small region of the short arm of chromosome 5 (5p)"

e. William syndrome-

Williams syndrome, which is associated with interstitial deletions of the long arm of chromosome 7 (7q11. 23); and the DiGeorge/velocardiofacial syndromes, associated with interstitial deletions of the long arm of chromosome 22 (22q11.2)

29. a) Myotonic dystrophy
b) Huntington chorea
d) Spinocerebellar ataxia

[Ref: Harrison 19th Edition; Harper 30th Edition]

a. Myotonic dystrophy

b. Huntington chorea

c. Ataxia telangiectasia

d. Spinocerebellar ataxia

e. Xeroderma pigmentosa

Trinucleotide sequences that increases in number (microsatellite instability) can cause disease. The unstable (CGG)n repeat sequence is associated with the fragile X syndrome. Other trinucleotide repeats that undergo dynamic mutation (usually an increase) are associated with Huntington's chorea (CAG), myotonic dystrophy (CTG), spinobulbar muscular atrophy (CA6), and Kennedy disease (CAG).

Selected Trinucleotide Repeat Disorders

Disease	Repeat	Inheritance	Gene Product
X-chromosomal spinobulbar muscular atrophy (SBMA)	CAG	XR	Androgen receptor
Fragile X-syndrome (FRAXA)	CSG	XR	FMR-1 protein
Fragile X-syndrome (FRAXE)	GCC	XR	FMR-2 protein
Dystrophia myotonica (DM)	CTG	AD, variable penetrance	Myotonin protein kinase
Huntingtons' disease (HD)	CAG	AD	Huntingtin

Spinocerebellar ataxia type 1 (SCA1)	CAG	AD	Ataxin 1
Spinocerebellar ataxia type 2 (SCA2)	CAG	AD	Ataxin 2
Spinocerebellar ataxia type 3 (SCA3); Machado-Joseph disease (MD)	CAG	AD	Ataxin 3
Spinocerebellar ataxia type 6 (SCA6, CACNAIA)	CAG	AD	Alpha 1A voltage-dependent L-type calcium channel
Spinocerebellar ataxia type 7 (SCA7)	CAG	AD	Ataxin 7
Spinocerebellar ataxia type 12 (SCA12)	CAG	AD	Protein phosphatase 2A
Dentorubral pallidoluysian atrophy (DRPLA)	CAG	AD	Atrophin 1
Friedreich (FRDA1)	GAA	AR	Frataxin

30. b) GTP
c) Initiation factor
e) mRNA

[Ref: Satyanarayan 4th Edition]

a. ATP-ATP does not form the part of the initiation complex.

b. GTP-

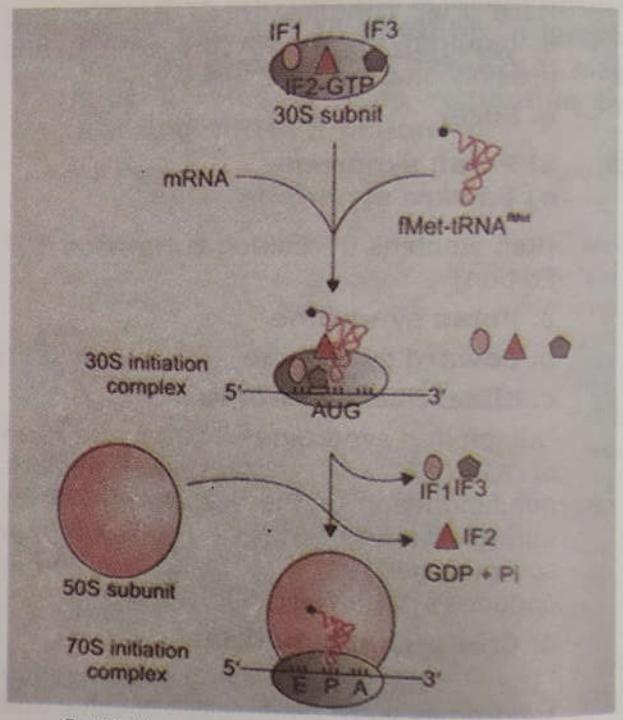
"30S initiation complex (30SIC) contains mRNA, fMet-tRNA^{fMat} and initiation factors IF1 and GTP-bound IF2"-www.nature.com

c. Initiation factor-

"In bacteria, during the initiation phase of protein synthesis three initiation factors (Ifs: IF1, IF2 and IF3), the messenger RNA (mRNA), and initiator tRNA (fMet-tRNA) assemble in a 30S pre-initiation complex (preIC) in which proper codon-anticodon base pairing has not ye takenplace"-academic. Oup.com

Initiation of translation in prokaryotes -The 30S ribosomal subunit is bound to initiation factor 3 (IF-3) and attached to ternary complex of IF-2, formyl met-tRNA and GTP

- Another initiation factor namely IF-1 also participates in the formation of preinitiation complex
- A 50S ribosome unit is now bound with 30S unit to produced 70S initiation complex



Initiation complex formation in bacteria

d. Elongation factor-elongation factor is required for elongation and not for initiation of the translation.

e. mRNA- Messenger RNA The specific mRNA required as a template for the synthesis of the desired polypeptide chain must be present. [Note: In eukaryotes, mRNA is circularized for use in translation.]

31. c) May result in 100 abnormal cells

[Ref: Harrison 19th]

a. No effect on organism-

- Some mutations may be lethal, others are less deleterious, and some may confer an evolutionary advantage.
- Mutations can occur in the germline (sperm or oocytes); these can be transmitted to progeny. Alternatively, mutations can occur during embryogenesis or in somatic tissues.
- Mutations that occur during development lead to mosaicism, a situation in which tissues are composed of cells with different genetic constitutions.

b. Every cell in the entire organism will be affected

In multicellular organisms, mutation: can be classed as either somatic or germline: ib. bioninja.com.au

- Somatic mutations: occur in a single body cell and cannot be inherited (only tissues derived from mutated cell are affected)
- Germline mutations: occur in gametes and can be passed onto offspring (every cell in the entire organism will be affected)

c. May result in 100 abnormal cells

As tissue (collection of cells) can be formed from mutant somatic cells option c (100 abnormal cells) may be true

d. Can be transmitted to progeny-

- If the germline is mosaic, a mutation can be transmitted to some progeny but not others, which sometimes leads to confusion in assessing the pattern of inheritance.
- Somatic mutations that do not affect cell survival can sometimes be detected because of variable phenotypic effects in tissues (e.g. pigmented lesions in McCune-Albright syndrome).
- Other somatic mutations are associated with neoplasia because they confer a growth advantage to cells. Epigenetic events may also influence gene expression or facilitate genetic damage. With the exception of triplet nucleotide repeats, which can expand, mutations are usually stable.

32. b) HGPRT transferase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Xanthine oxidase-

Hypouricemia and increased excretion of hypoxanthine and xanthine are associated with xanthine oxidase deficiency due to a genetic defect or to severe liver damage. Patients with a severe enzyme deficiency may exhibit xanthinuria and xanthine lithiasis.

b. HGPRT transferase

Lesch Nyhan Syndrome

- X-linked recessive disorder with complete absence of HGPRTase enzyme of purine salvage pathway. Enzymes of de novo synthesis of purines are absent in brain. Therefore brain is dependent entirely upon salvage pathway.
- **Reason for hyperuricemia:**
- HGPRTase enzyme reutilises (salvages) purine bases. When these enzyme is deficient, guanine, xanthine or hypoxanthine are not slavaged and therefore degraded to uric acid resulting in hyperuricemia.
- **Clinical Features:**
- Affected children are usually male.
- Hyperuricemia.
- Spasticity, Mental retardation.
- Self-mutation* - Biting tongue, fingers, chewing lips – striking feature of this disease.
- **Treatment:**
- No curative treatment is available. Removal of deciduous teeth is done to avoid injury. Other managements are symptomatic.
- Genetic counselling and carrier testing for prevention.

c. PRPP synthetase-

In normal circumstances, PRPP synthetase is under feedback control by purine nucleotides (ADP and CDP). However, variant forms of PRPP synthetase-which are not subjected to feedback regulation-have been detected. This leads to the increased production of purines.

d. Orotic acid dehydrogenase-This is enzyme of pyrimidine biosynthesis.

33. b) To map the location of mutant genes

[Ref: Harper's Illustrated biochemistry, 30th Edition]

- Gene localization can define a map of the human genome.
- Two techniques used to accomplish this
- Somatic cell hybridization
- In situ hybridization.
- In situ hybridization
- Simpler and more direct procedure.
- A radioactive probe is added to a metaphase spread of chromosomes on a glass slide.
- The exact area of hybridization is localized by layering photographic emulsion over the slide and, after exposure, lining up the grains with some histologic identification of the chromosome.
- Fluorescence in situ hybridization (FISH)
- Utilizes fluorescent rather than radioactively labelled probes, is a very sensitive technique.
- This often places the gene at a location on a given band or region on the chromosome.
- Once the defect is localized to a region of DNA that has the characteristic structure of a gene, a synthetic cDNA copy of the gene can be constructed, which contains only mRNA encoding exons, and expressed in an appropriate vector and its function can be assessed-or the putative polypeptide, deduced from the open reading frame in the coding region, can be synthesized.
- Antibodies directed against this protein or peptide fragments derived therefrom can be used to assess whether this protein is expressed in normal persons and whether it is absent, or altered in those with the genetic syndrome.

34. b) Increased cell division

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Telomeres

- Structures at the ends of chromosome that contain multiple repeats of specific hexanucleotide DNA sequences.
- The telomeres of normal cells shorten on repeated cell division, which may result in cell death.
- The enzyme telomerase replicates telomeres and is often expressed in cancer cells, helping them to evade cell death.
- Telomerase is usually not detected in normal somatic cells.
- The telomeres provide an innocuous source of DNA whose decreasing length if of little immediate consequence to the cell. However, once the supply of telomere DNA is exhausted, roughly 100 cell divisions for humans, mitosis ceases and the somatic cell enters a state of replicative senescence. As more and more cells within the body enter senescence, it progressively loses the capacity to replace lost or damaged cells.
- Organisms are able to generate progeny that contain full length telomeres thanks to the intervention of the enzyme telomerase.
- Telomerase is a ribonucleoprotein that is expressed in stem cells and most cancer cells, but not in somatic cells.
- Using an RNA template, telomerase adds GT-rich hexanucleotide repeat sequences ranging from a few hundred (yeast) to several thousand (humans) nucleotides in length to the ends of linear DNA molecules to restore their telomeres to full length.
- When somatic cells are genetically engineered in the laboratory to express telomerase, they continue to divide in culture long after an unaltered control cell line stops.

Note:

- Cells with telomerase activity
- Germinal cells
- Cancer cells
- Stem cells
- Cells without telomerase activity
- Somatic cells

35. a) Directly proportional to GC pairing

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Explanation:

- The strands of a given molecule of DNA separate over a temperature range. The midpoint is called the melting temperature, or Tm.
- The Tm is influenced by the base composition of the DNA and by the salt concentration of the solution.
- DNA rich in G-C pairs, which have three hydrogen bonds, melts at a higher temperature than that rich in A-T pairs, which have two hydrogen bonds.
- A 10-fold increase of monovalent cation concentration increases the Tm by 16.6°C by neutralizing the intrinsic interchain repulsion between the highly negatively charged phosphates of the phosphodiester backbone.
- Conversely, the organic solvent formamide, which is commonly used in recombinant DNA experiments, destabilizes hydrogen bonding between bases, thereby lowering the Tm.
- Formamide addition allows the strands of DNA or DNA-RNA hybrids to be separated at much lower temperatures and minimizes the phospodiester bond breakage that can occur upon extended incubation at higher temperatures.

36. c) For t-RNA ribosomal binding

[Ref: Lippincott Biochemistry, 6th edition]

Function of t-RNA

Limbs of t-RNA	Function
TΨC arm (Ribothymidine pseudouridine cytidine arm)	Binding of aminoacyl-t-RNA to ribosomal surface at the site of protein synthesis
D arm	Recognition of t-RNA to the enzyme aminoacyl t-RNA synthatase
Acceptor arm	Site of attachment of specific amino acid
Anticodon arm	Antiparallel to the coding sequence of amino acid on the m-RNA

37. a) PRPP glutamine amidotransferase

[Ref: Textbook of Medical Biochemistry by Chatterjea and Shinde, 8th edition]

Explanation:

- **PRPP synthetase**
- It is an important enzyme that regulates purine synthesis.
- It is allosterically inhibited by PRPP and number of purine nucleotides.
- Glutamine PRPP amidotransferase
- Is the enzyme for the rate-limiting step of purine synthesis.
- It is regulated by feedback inhibitory effects of AMP and GMP.
- A proper balance between the Adenine and guanine concentration is maintained by adenylosuccinate synthetase and IMP dehydrogenase respectively.

38. b) DNA sequencing

[Ref: Harper's Illustrated Biochemistry, 30th edition& Lehninger, Principles of Biochemistry, 6th edition]

Explanation:

Single Nucleotide Polymorphisms (SNP)

- Within the human population are millions of single-base differences, called single nucleotide polymorphisms or SNPs (pronounced "snips").
- SNP refers to the fact that single nucleotide genetic variation in genome sequence exists at discrete loci throughout the chromosomes.
- SNP detection technologies are used to scan for new polymorphisms and to determine the allele of a known polymorphism in target sequences.
- Driven by the Human Genome Project, these technologies are now maturing and robust strategies are found in both SNP discovery and genotyping areas.
- Local, target, SNP discovery relies mostly on direct DNA sequencing or on denaturing high performance liquid chromatography (dHPLC).
- The catch in this question is the phrase without a prior sequence

information.....that rules out microarray as a DNA microarray (also commonly known as DNA chip or biochip) is a collection of microscopic DNA spots attached to a solid surface.

- Scientists use DNA microarrays to measure the expression levels of large numbers of genes simultaneously or to genotype multiple regions of a genome.
- Each DNA spot contains picomoles (10-12 moles) of a specific DNA sequence, known as probes (or reporters or oligos).

39. a) Northern blot

[Ref: Harper's Illustrated Biochemistry, 29th edition]

Explanation:

Northern blot: A method for transferring RNA from an agarose gel to nitrocellulose filter, on which RNA can be detected by probe.

Techniques	Used for
Northern blot	RNA Analysis
Southern blot	DNA Analysis
Western blot	Protein Analysis
South-western blot	Protein-DNA interactions

40. d) All of the above

The nucleus of the eukaryotic cell contains a dense body known as nucleolus. It is rich in RNA, particularly the ribosomal RNA which enters the cytosol through nuclear pores.

The ground material of the nucleus is often referred to as nucleoplasm. It is rich in enzymes such as DNA polymerases and RNA polymerases. To the surprise of biochemists, the enzymes of glycolysis, citric acid cycle and hexose monophosphate shunt have also been detected in the nucleoplasm. The mitochondrial matrix contains a circular double stranded DNA (mtDNA), RNA and ribosomes. Thus, the mitochondria are equipped with an independent protein synthesizing machinery. It is estimated that about 10% of the mitochondrial oroteins are produced in the mitochondria.

41. a) Severe combined immuno-deficiency

[Ref: Harper's Illustrated Biochemistry, 30th edition]

Adenosine deaminase (ADA) deficiency causing severe combined immunodeficiency disease (SCID)

Causation- Genetic (due to mutations in the gene encoding ADA). Deficiency of ADA affects the immune system.

Laboratory Findings -

Analysis of a sample of red blood cells revealed a very low activity of ADA and also a very high level (about 50 times normal) of dATP.

Mutations in the gene for ADA located on chromosome 20

↓

Deficient activity of ADA

↓

Increased levels of adenosine, deoxyadenosine and dATP

↓

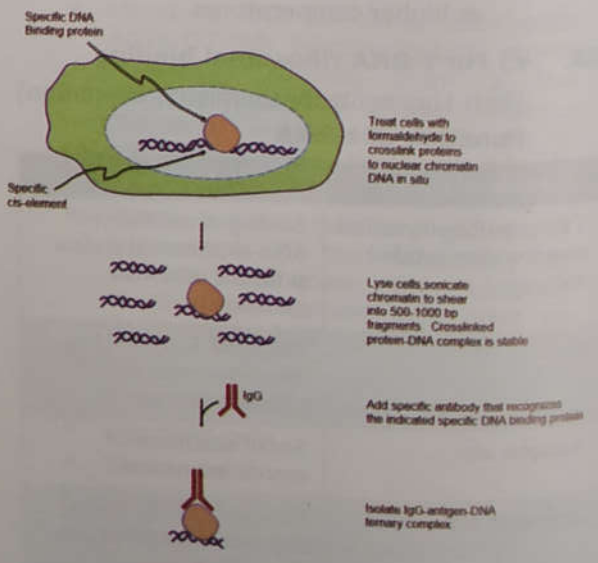
Toxicity to lymphocytes

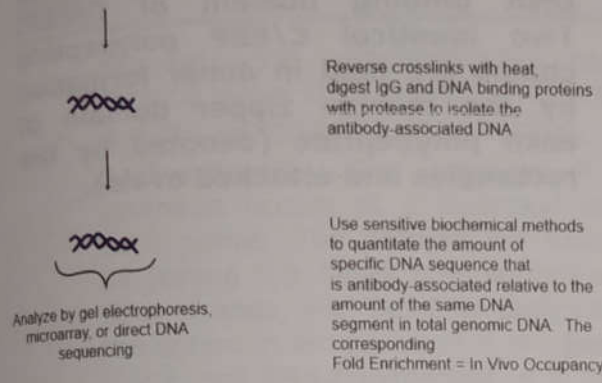
↓

Decreased synthesis of immunoglobulins and impaired cell-mediated immunity

42. d) ChIP on chip

[Ref: Harper's Illustrated Biochemistry, 30th edition]


Specific DNA Binding protein
Specific cis-element
Treat cells with formaldehyde to crosslink proteins to nuclear chromatin DNA in situ
Lyse cells,sonicate chromatin to shear into 500-1000 bp fragments. Crosslinked protein-DNA complex is stable
IgG
Add specific antibody that recognizes the indicated specific DNA binding protein
Isolate IgG-antigen-DNA ternary complex


Reverse crosslinks with heat, digest IgG and DNA binding proteins with protease to isolate the antibody-associated DNA
Use sensitive biochemical methods to quantitate the amount of specific DNA sequence that is antibody-associated relative to the amount of the same DNA segment in total genomic DNA. The corresponding Fold Enrichment = In Vivo Occupancy
Analyze by gel electrophoresis, microarray, or direct DNA sequencing

Outline of the chromatin immunoprecipitation (ChIP) technique.

43. d) All of the above

DNA FINGERPRINTING OR DNA PROFILING

DNA fingerprinting is the present day genetic detective in the practice of modern medical forensics. The underlying principles of DNA fingerprinting are briefly described.

The structure of each person's genome is unique. The only exception being monozygotic identical twins (twins developed from a single fertilized ovum). The unique nature of genome structure provides a good opportunity for the specific identification of an individual.

It may be remembered here that in the traditional fingerprint technique, the individual is identified by preparing an ink impression of the skin folds at the tip of the person's finger. This is based on the fact that the nature of these skin folds is genetically determined, and thus the fingerprint is unique for an individual. In contrast, the DNA fingerprint is an analysis of the nitrogenous hase sequence in the DNA of an individual.

44. c) Cistron

The cistron is the smallest unit of genetic expression. Thus, the "one gene, one enzyme" concept is not necessarily valid. The cistron is the genetic unit coding for the structure of the subunit of a protein molecule, acting as it does as the smallest unit of genetic expression. Thus, the one gene, one enzyme idea might more accurately be regarded as a one cistron, one subunit concept. A single mRNA that encodes more than one separately translated protein is referred to as a polycistronic mRNA. For example, the polycistronic lac operon mRNA is translated into three separate proteins . Operons and polycistronic mRNAs are common in bacteria but not in eukaryotes.

45. b) snRNA

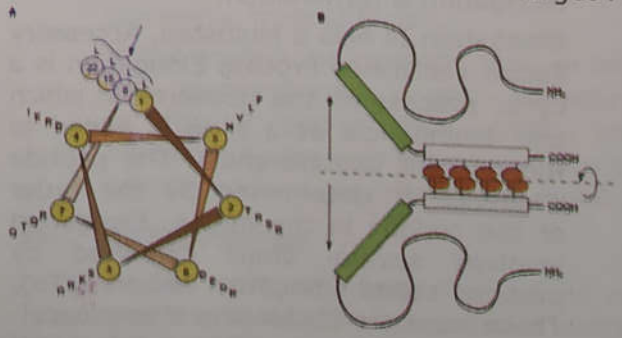
snRNA: Small nuclear RNA. This family of RNAs is best known for its role in mRNA processing.

Spliceosome: The macromolecular complex responsible for precursor mRNA splicing. The spliceosome consists of at least five small nuclear RNAs (snRNA; U1, U2, U4, U5, and U6) and many proteins.

46. e) 7 amino acid

[Ref: Harper's Illustrated biochemistry, 29th Edition]

The Leucine Zipper Motif Careful analysis of a 30-amino-acid sequence in the carboxyl terminal region of the enhancer binding protein C/EBP revealed a novel structure, the leucine zipper motif, this region of the protein forms an α helix in which there is a periodic repeat of leucine residues at every seventh position. This occurs for eight helical turns and four leucine repeats. Similar structures have been found in a number of other proteins associated with the regulation of transcription in mammalian and yeast cells. This structure allows two identical or nonidentical monomers (eg, Jun-Jun or Fos-Jun) to "zip together" in a coiled coil and form a tight dimeric complex. This protein-protein interaction may serve to enhance the association of the separate DNA binding domains with their target .



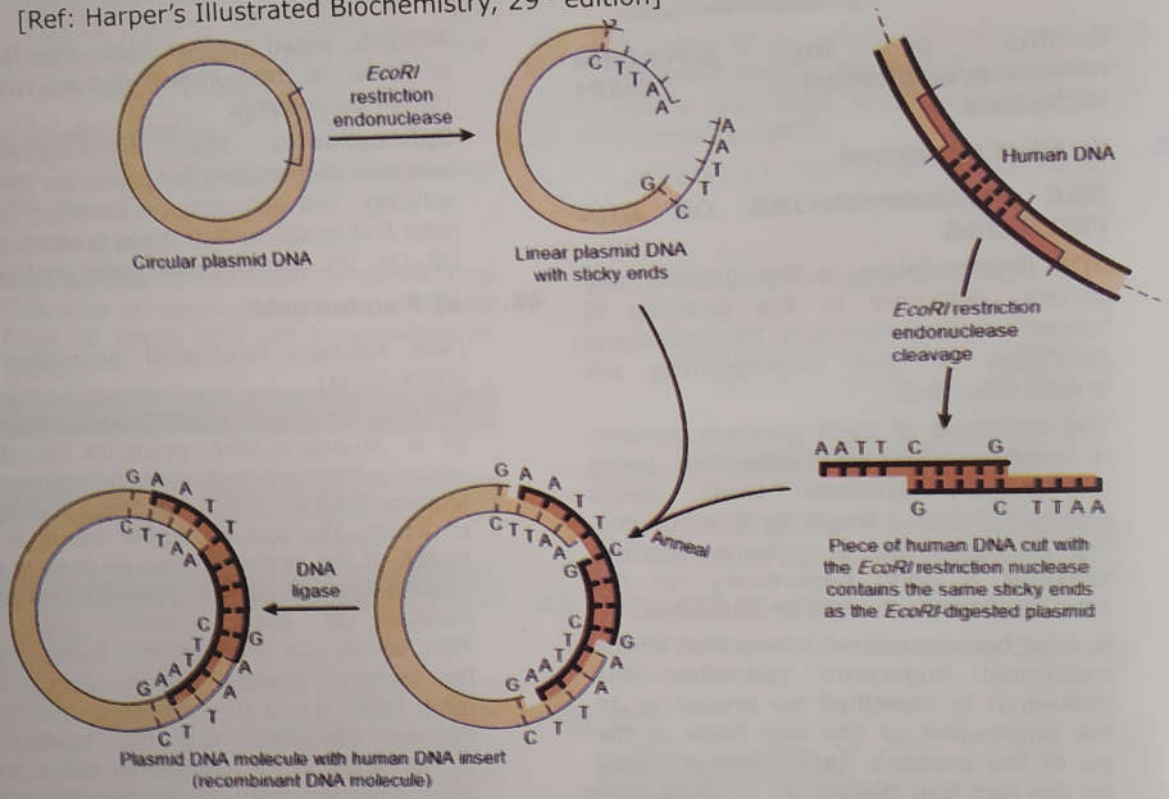
The leucine zipper motif.

(A) shows a helical wheel analysis of a carboxyl terminal portion of the DNA binding protein C/EBP. Note that leucine residues (L) occur at every seventh position (in this schematic C/EBP amino acid residues 1, 8, 15, 22; see arrow).

(B) is a schematic model of the DNA binding domain of C/EBP. Two identical C/EBP polypeptide chains are held in dimer formation by the leucine zipper domain of each polypeptide (denoted by the rectangles and attached ovals).

47. a) Transformation

[Ref: Harper's Illustrated Biochemistry, 29th edition]


EcoRI restriction endonuclease
Circular plasmid DNA
Linear plasmid DNA with sticky ends
Human DNA
EcoRI restriction endonuclease cleavage
AATT C G
G C TTAA
Piece of human DNA cut with the EcoRI restriction nuclease contains the same sticky ends as the EcoRI-digested plasmid
Anneal
DNA ligase
Plasmid DNA molecule with human DNA insert (recombinant DNA molecule)

Use of restriction nucleases to make new recombinant or chimeric DNA molecules.

48. d) Elongation of proteins

Like transcription, protein synthesis can be described in three phases: initiation, elongation & termination:

Elongation Is Also a Multistep, Accessory Factor-Facilitated Process Elongation is a cyclic process on the ribosome in which one amino acid at a time is added to the nascent peptide chain. The peptide sequence is determined by the order of the codons in the mRNA. Elongation involves several steps catalyzed by proteins called elongation factors (EFs). These steps are (1) binding of aminoacyl-tRNA to the A site, (2) peptide bond formation, and (3) translocation of the ribosome on the mRNA.

49. c) Magnesium

[Ref: Satyanarayan 4th Edition]

The actual technique of PCR involves repeated cycles for amplification of target DNA. Each cycle has three stages.

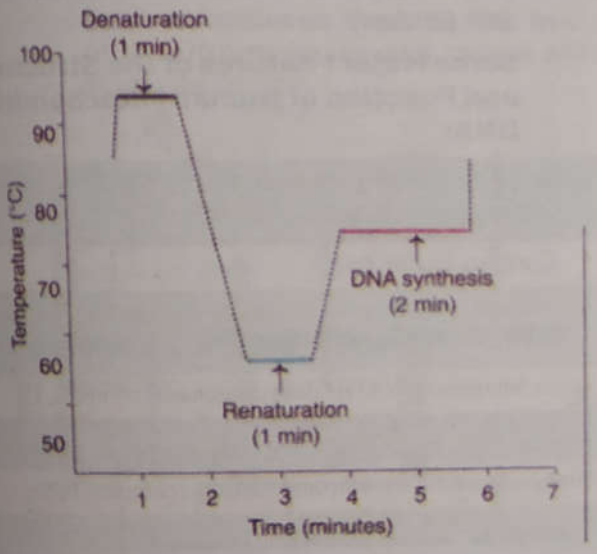
1. Denaturation : On raising the temperature to about 95oC for about one minute, the DNA gets denatured and the two strands separate.

2. Renaturation or annealing : As the temperature of the mixutre is slowly cooled to about 55oC, the primers base

pair with the complementary regions flanking target DNA strands. This process is called renaturation or annealing.

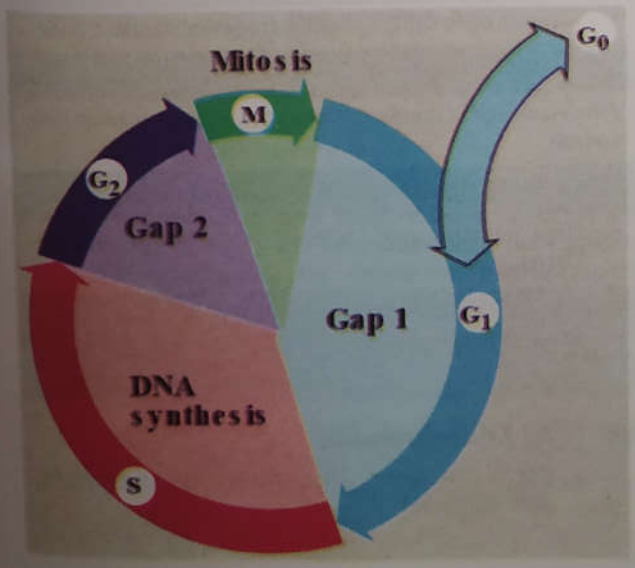
3. Synthesis : The initiation of DNA synthesis occurs at 3'-hydroxyl end of each primer. The primers are extended by joining the bases complementary to DNA strands, For Taq DNA polymerase, the optimum temperature is around 75'C (for E. coli DNA polymerase, it is around 37"C). The reaction can be stopped by raising the temperature (to about 95'C).

The 3 stages of PCR in relation to temperature and time are depicted in



50. b) M

[Ref: Lippincott's illustrated reviews, 6th Edition]



The eukaryotic cell cycle. [Note: Cells can leave the cell cycle and enter a reversible quiescent state called G0.]

Radio sensitive is M Phase.

51. a) AUG

Twenty different amino acids are required for the synthesis of the cellular complement of proteins; thus, there must be at least 20 distinct codons that make up the genetic code.The terms first, second, and third nucleotide refer to the individual nucleotides of a triplet codon. U, uridine nucleotide; C, cytosine nucleotide; A, adenine nucleotide; G, guanine nucleotide; Term, chain terminator codon. AUG, which codes for Met, serves as the initiator codon in mammalian cells and also encodes for internal methionines in a protein. In mammalian mitochondria, AUA codes for Met and UGA for Trp, and AGA and AGG serve as chain terminators.

52. c) RNA

In a Southern, or DNA, blot transfer, DNA isolated from a cell line or tissue is digested with one or more restriction enzymes. This mixture is pipetted into a well in an agarose or polyacrylamide gel and exposed to a direct electrical current. DNA, being negatively charged, migrates toward the anode; the smaller fragments move the most rapidly.

The RNA, or Northern, blot is conceptually similar. RNA is subjected to electrophoresis before blot transfer. This requires some different steps from those of DNA transfer, primarily to ensure that the RNA remains intact, and is generally somewhat more difficult.

In the protein, or Western, blot, proteins are electrophoresed and transferred to special paper that avidly binds macromolecules and then probed with a specific antibody or other probe molecule.

53. d) Microarray

In the case of microarrays, it is now possible to deposit thousands of specific, known, definable DNA sequences (more typically now synthetic oligonucleotides)

on a glass microscope-style slide in the space of a few square centimeters. By coupling such DNA microarrays with highly sensitive detection of hybridized fluorescently labeled nucleic acid probes derived from mRNA, investigators can rapidly and accurately generate profiles of gene expression (eg, specific cellular mRNA content) from cell and tissue samples as small as 1 g or less. Thus entire transcriptome information (the entire collection of cellular mRNAs) for such cell or tissue sources can readily be obtained in only a few days. In the case of NGS sequencing, mRNAs are converted to cDNAs using reverse transcription, and these cDNAs are directly sequenced.

Microarray techniques, high-throughput DNA sequencing, two-hybrid genetic knockdown, and mass spectrometric protein and metabolite identification experiments have led to the generation of huge amounts of data.

54. c) Nucleic acid

PCR has become a very common tool for a large number of applications.

1. Comparison of a normal gene with a mutant form of the gene: PCR allows the synthesis of mutant DNA in sufficient quantities for a sequencing protocol without laboriously cloning the altered DNA.

2. Detection of low-abundance nucleic acid sequences: Viruses that have a long latency period, such as human immunodeficiency virus (HIV), are difficult to detect at the early stage of infection using conventional methods. PCR offers a rapid and sensitive method for detecting viral DNA sequences even when only a small proportion of cells harbors the virus.

3. Forensic analysis of DNA samples: DNA fingerprinting by means of PCR has revolutionized the analysis of evidence from crime scenes. DNA isolated from a single human hair, a tiny spot of blood, or a sample of semen is sufficient to determine whether the sample comes from a specific individual. The DNA markers analyzed for such fingerprinting are most commonly short tandem repeat polymorphisms. These are very similar to the VNTRs described previously but are smaller in size. [Note: Determination of paternity uses the same techniques.]

4. Prenatal diagnosis and carrier detection of cystic fibrosis: Cystic fibrosis is an autosomal recessive genetic disease resulting from mutations in the gene for the cystic fibrosis transmembrane conductance regulator (CFTR) protein.

55. b) Maternally transmitted

[Ref: Harper's Illustrated biochemistry, 30th Edition]

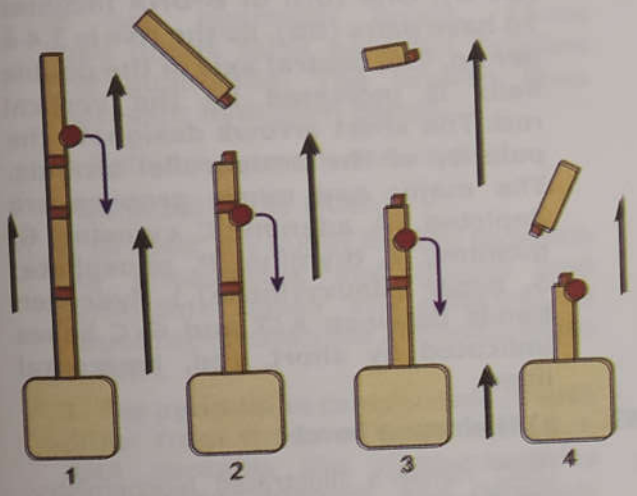
Some Major Features of the Structure and Function of Human Mitochondrial DNA:

• Is circular, double-stranded, and composed of heavy (H) and light(L) chains or strands
• Contains 16,569 bp
• Encodes 13 protein su bun its of the respiratory chain (of a total ofabout 67)
Seven subunits of NADH dehydrogenase (complex 1)
Cytochrome b of complex III
Three subunits of cytochrome oxidase (complex IV)
Two subunits of ATP synthase
• Encodes large (16S) and small (12$) mt ribosomal RNAs
• Encodes 22 mttRNA molecules-
• Genetic code differs slightly from the standard code
UGA (standard stopcodon) is read asTrp
AG A and AGG (standard codons for Arg) are read as stop codons
• Contains very few untranslated sequences-
• High mutation rate (5 to 10 times that of nuclear DNA)
• Comparisons of mtDNA sequences provide evidence about evolutionary origins of primates and other species

56. a) Endonuclease

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Direct observation of single DNA cleavage events catalyzed by a restriction endonuclease. DNA molecules immobilized to beads (pale yellow) are placed in a flowing stream of buffer (black arrows), which causes them to assume an extended conformation. Cleavage at one of the restriction sites (orange) by an endonuclease leads to a shortening of the DNA molecule, which can be observed directly in a microscope since the nucleotide bases in DNA are fluorescent. Although the endonuclease (red) does not fluoresce, and hence is invisible, the progressive manner in which the DNA molecule is shortened (1→4) reveals that the endonuclease binds to the free end of the DNA molecule and moves along it from site to site.



57. c) Acrocentric

RT-PCR is used for all except
a. Complimentary DNA cloning
b. cDNA library construction
c. Amplify and quantify a target sequence
d. Probe synthesis

RT-PCR: A method used to quantitate mRNA levels that relies upon a first step of cDNA copying of mRNAs catalyzed by reverse transcriptase prior to PCR amplification and quantitation.

58. c) FISH

FISH: Fluorescence in situ hybidization, a method used to map the location of specific DNA sequences within fixed nuclei.

Fluorescence in situ hybridization (FISH), which utilizes fluorescent rather than radioactively labeled probes, is a very sensitive technique that is also used for this purpose. This often places the gene at a location on a given band or region on the chromosome.

59. b) 0.02%

In Human DNA, at Least 30% of the Genome Consists of Repetitive Sequences Repetitive-sequence DNA can be broadly classified as moderately repetitive or as highly repetitive. The highly repetitive sequences consist of 5–500 base pair lengths repeated many times in tandem. These sequences are often clustered in centromeres and telomeres of the chromosome and some arepresent in about 1–10 million copies per haploid genome. The majority of these sequences are transcriptionally inactive and some of these sequences play a structural role in the chromosome.

60. a) A+G = T+C

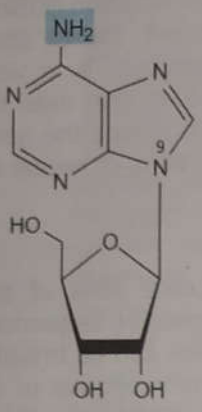
Chargaff rules! Biochemist Erwin Chargaff was the first to note that, in DNA, [A] = [T] and [G] = [C], equalities now called Chargaff's rule.

The specific base-pairing in DNA leads to the Chargaff rule, which states that in any sample of dsDNA, the amount of A equals the amount of T, the amount of G equals the amount of C, and the total amount of purines equals the total amount of pyrimidines.

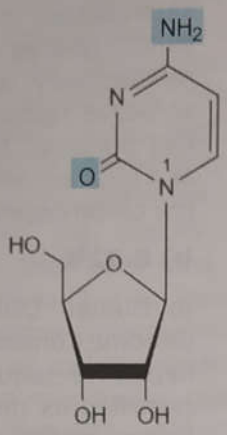
61. b) Nucleoside

[Ref: Harper's Illustrated biochemistry, 30th Edition]

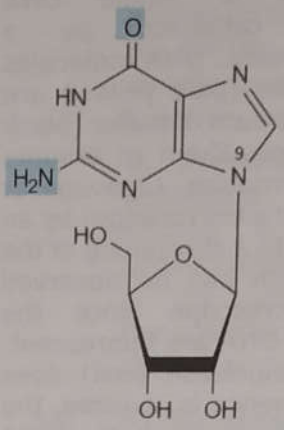
Nucleosides Are N-Glycosides Nucleosides are derivatives of purines and pyrimidines that have a sugar linked to a ring nitrogen of a purine or pyrimidine. Numerals with a prime (eg, 2' or 3') distinguish atoms of the sugar from those of the heterocycle. The sugar in ribonucleosides is D-ribose, and in deoxyribonucleosides is 2-deoxy-D-ribose. Both sugars are linked to the heterocycle by a β-n-glycosidic bond, almost always to the N-1 of a pyrimidine or to N-9 of a purine.



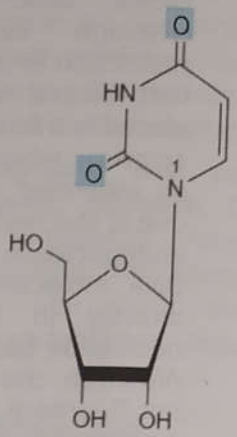
Adenosine



Cytidine



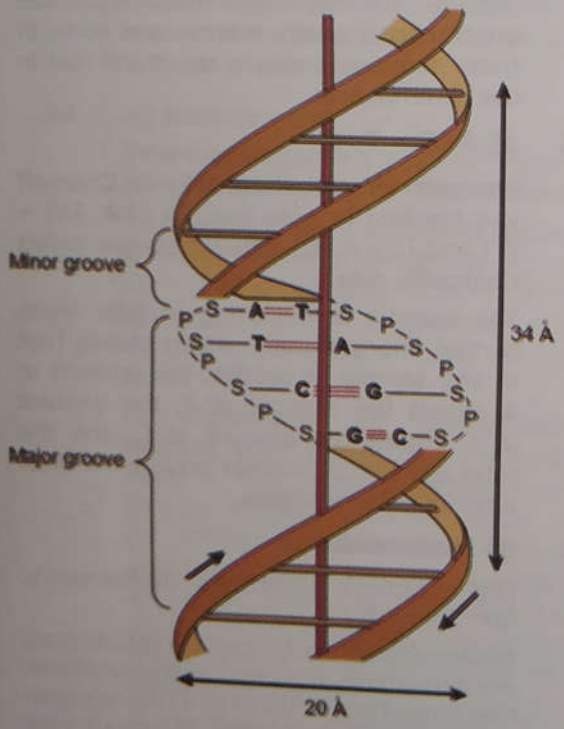
Guanosine



Uridine

62. b) G-C

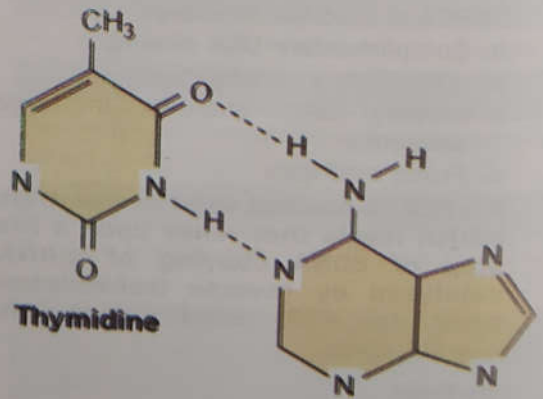
[Ref: Harper's Illustrated biochemistry, 30th Edition]



A diagrammatic representation of the Watson and Crick model of the double-helical structure of the B form of DNA. The horizontal arrow indicates the width of the double helix (20 Å), and the vertical arrow indicates the distance spanned by one complete turn of the double helix (34 Å). One turn of B-DNA includes 10 base pairs (bp), so the rise is 3.4 Å per bp. The central axis of the double helix is indicated by the vertical rod. The short arrows designate the polarity of the antiparallel strands. The major and minor grooves are depicted. (A, adenine; C, cytosine; G, guanine; T, thymine; P, phosphate; S, sugar [deoxyribose].) Hydrogen bonds between A/T and G/C bases indicated by short, red, horizontal lines.

63. a) Hydrogen bond

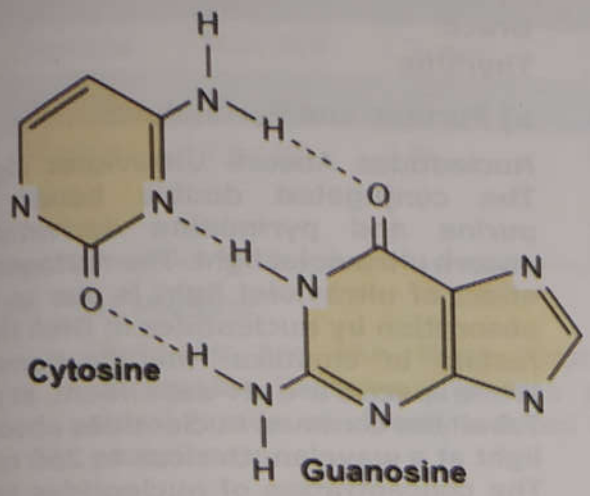
[Ref: Harper's Illustrated biochemistry, 30th Edition]



Thymidine

Adenosine

64.



DNA base pairing between adenosine and thymidine involves the formation of two hydrogen bonds. Three such bonds form between cytidine and guanosine. The broken lines represent hydrogen bonds.

64. d) Dehydroxy-methyltaurine

Ribonucleic acid (RNA):

1. In RNA, the sugar moiety to which the phosphates and purine and pyrimidine bases are attached is ribose rather than the 2′-deoxyribose of DNA.

2. The pyrimidine components of RNA differ from those of DNA. Although RNA contains the ribonucleotides of adenine, guanine, and cytosine, it does not possess thymine except in the rare case mentioned below. Instead of thymine, RNA contains the ribonucleotide of uracil.

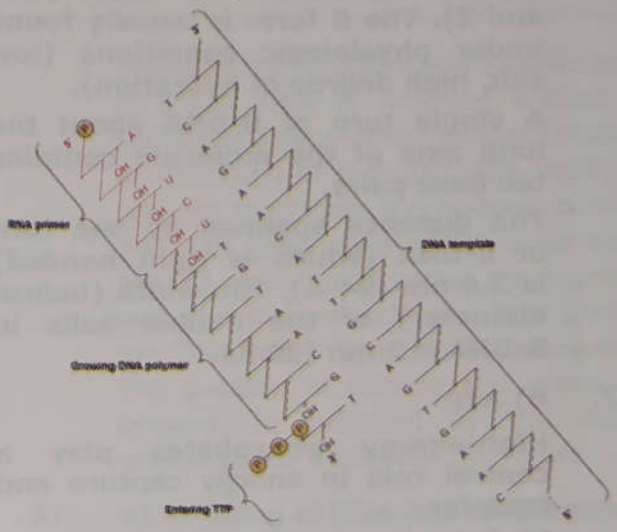
3. RNA typically exists as a single strand, whereas DNA exists as a double-stranded helical molecule.

4. Since the RNA molecule is a single strand complementary to only one of the two strands of a gene, its guanine content does not necessarily equal its cytosine content, nor does its adenine content necessarily equal its uracil content.

5. RNA can be hydrolyzed by alkali to 2′,3′ cyclic diesters of the mononucleotides, compounds that cannot be formed from alkali-treated DNA because of the absence of a 2′-hydroxyl group. The sequence of the RNA molecule (except for U replacing T) is the same as that of the coding strand of the gene.

65. b) Watson & Crick

[Ref: Harper's Illustrated biochemistry, 30th Edition]



The RNA-primed synthesis of DNA demonstrating the template function of the complementary strand of parental DNA.

DNA molecule according to the rules proposed originally by Watson and Crick.

66. a) Right handed anti parallel

[Ref: Harper's Illustrated biochemistry, 30th Edition]

DNA Contains Four Deoxynucleotides The chemical nature of the monomeric deoxynucleotide units of DNA—deoxyadenylate, deoxyguanylate, deoxycytidylate, and thymidylate.

Watson, Crick, and Wilkins to propose in the early 1950s a model of a double-stranded DNA molecule. The model they proposed has pairings between the purine and pyrimidine nucleotides on the opposite strands are very specific and are dependent upon hydrogen bonding of A with T and G with C .

The two strands of the double-helical molecule, each of which possesses a polarity, are antiparallel; ie, one strand runs in the 5′ to 3′ direction

and the other in the 3′ to 5′ direction.

The two strands, in which opposing bases are held together by interstrand hydrogen bonds, wind around a central axis in the form of a double helix.

In the test tube doublestranded DNA can exist in at least six forms (A–E and Z). The B form is usually found under physiologic conditions (low salt, high degree of hydration).

A single turn of B-DNA about the long axis of the molecule contains ten base pairs.

The distance spanned by one turn of B-DNA (which is right handed) is 3.4 nm (34 Å). The width (helical diameter) of the double helix in B-DNA is 2 nm (20 Å).

67. b) ATP

High-energy phosphates play a central role in energy capture and transfer

High-Energy Phosphates Are Designated by ~P The symbol ~P indicates that the group attached to the bond, on transfer to an appropriate acceptor, results in transfer of the larger quantity of free energy. For this reason, the term group transfer potential, rather than "high-energy bond," is preferred by some. Thus, ATP contains two high-energy phosphate groups and ADP contains one, whereas the phosphate in AMP (adenosine monophosphate) is of the low-energy type, since it is a normal ester link.

68. b) ADP

A Membrane-Located ATP Synthase Functions as a Rotary Motor to Form ATP The proton motive force drives a membrane-located ATP synthase that in the presence of Pi + ADP forms ATP.

69. c) Guanine

Purines:
adenine
guanine
Pyrimidines:
Cytosine
Uracil
Thymine

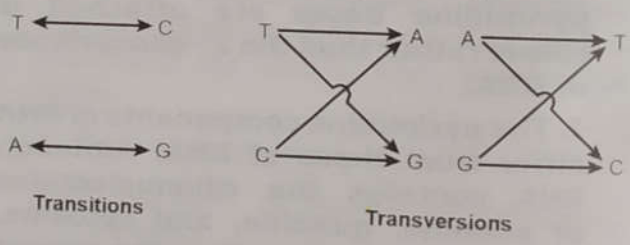
70. a) Purines and Pyrimidines

Nucleotides Absorb Ultraviolet Light The conjugated double bonds of purine and pyrimidine derivatives absorb ultraviolet light. The mutagenic effect of ultraviolet light is due to its absorption by nucleotides in DNA that results in chemical modifications . While spectra are pH-dependent, at pH 7.0 all the common nucleotides absorb light at a wavelength close to 260 nm. The concentration of nucleotides and nucleic acids thus often is expressed in terms of "absorbance at 260 nm."

71. a) Guanine-cytosine
c) Guanine-thymine
d) Adenine-thymine

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Transversions are changes from a purine to either of the two pyrimidines or the change of a pyrimidine into either of the two purines,:



Diagrammatic representation of transition mutations and transversion mutations

72. c) Jeffery

73. a) 5.8 S
e) 28 S

[Ref: Harper's Illustrated biochemistry, 29th Edition]

The components of the mammalian ribosome, which has a molecular weight of about 4.2 × 106 and a sedimentation velocity coefficient of 80S (S = Svedberg units, a parameter sensitive to molecular size and shape) are shown:

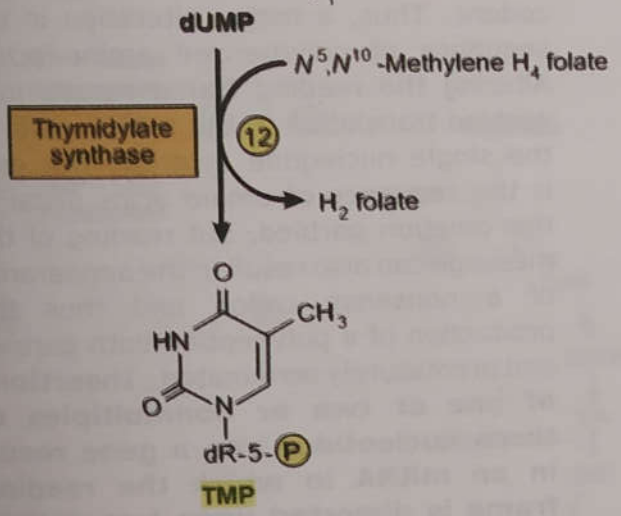
		Protein		RNA		
Component	Mass (MW)	Number	Mass	Size	Mass	Bases
40S subunit	1.4×10^6	33	7×10^5	18S	7×10^5	1900
60S subunit	2.8×10^6	50	1×10^6	5S	35,000	120
				5.8S	45,000	160
				28S	1.6×10^6	4700

74. b) Histone

Histones Are the Most Abundant Chromatin Proteins Histones are a small family of closely related basic proteins.

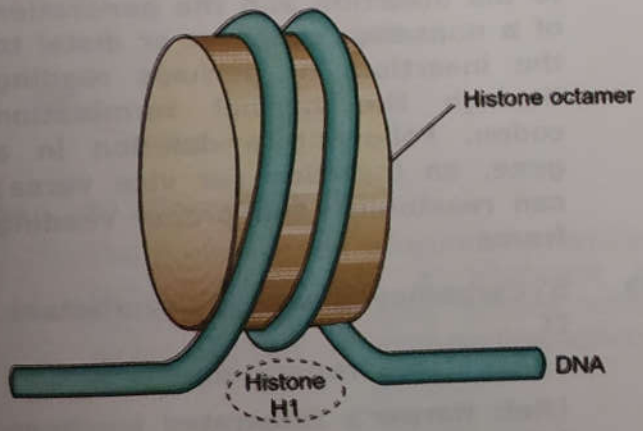
75. a) N 5, N 10-methylene tetrahydrofolate

[Ref: Harper's Illustrated biochemistry, 29th Edition]



76. c) Regular repeating structure of DNA & histone proteins

[Ref: Harper's Illustrated biochemistry, 29th Edition]



Model for the structure of the nucleosome, in which DNA is wrapped around the surface of a flat protein cylinder consisting of two each of histones H2A, H2B, H3, and H4 that form the histone octamer. The 146 base pairs of DNA, consisting of 1.75 superhelical turns, are in contact with the histone octamer. This protects the DNA from digestion by a nuclease. The position of histone H1, when it is present, is indicated by the dashed outline at the bottom of the figure.

77. a) Splitting of DNA into single strands

The Denaturation of DNA Is Used to Analyze Its Structure

The double-stranded structure of DNA can be separated into two component strands in solution by increasing the temperature or decreasing the salt concentration. Not only do the two stacks of bases pull apart but the bases themselves unstack while still connected in the polymer by the phosphodiester backbone. Concomitant with this denaturation of the DNA molecule is an increase in the optical absorbance of the purine and pyrimidine bases—a phenomenon referred to as hyperchromicity of denaturation. Because of the stacking of the bases and the hydrogen bonding between the stacks, the double-stranded DNA molecule exhibits properties of a rigid rod and in solution is a viscous material that loses its viscosity upon denaturation. The strands of a given molecule of DNA separate over a temperature range. The midpoint is called the melting temperature, or Tm. The Tm is influenced by the base composition of the DNA and by the salt concentration of the solution.

78. d) Amplify a small amount of DNA

Applications of pcr:

PCR in clinical diagnosis:These include diagnosis of inherited disorders (genetic diseases), viral diseases, bacterial diseases etc.

Prenatal diagnosis of inherited diseases

Diagnosis of retroviral infections

Diagnosis of bacterial infections

Diagnosis of cancers

PCR in sex determination of embryos

PCR in DNA sequencing

PCR in comparative studies of genomes

PCR in forensic medicine

79. b) Overlapping
c) Ambiguous
d) Universal

The genetic code is

- **Degenerate,**
- **Unambiguous,**
- **Nonoverlapping,**
- **Without punctuation, &**
- **Universal**

80. a) UGA codes for tryptophan
b) Codes for 13 protein
d) Circular double stranded DNA
e) Mitochondrial disease occur due to point mutation and large scale rearrangements

81. b) Primase

[Ref: Harper's Illustrated biochemistry, 29th Edition]

Protein	Function
DNA Polymerases	Deoxynucleotide polymerization
Helicases	Processive unwinding of DNA
Topoisomerases	Relieve torsional strain that results from helicase-induced unwinding
DNA primase	Initiates synthesis of RNA primers
Single-Strand binding proteins	Prevent premature reannealing of dsDNA
DNA ligase	Seals the single strand nick between the nascent chain and Okazaki fragments on lagging strand

Primosome: The mobile complex of helicase and primase that is involved in DNA replication.

82. b) Translation

[Ref: Harper's Illustrated biochemistry, 29th Edition]

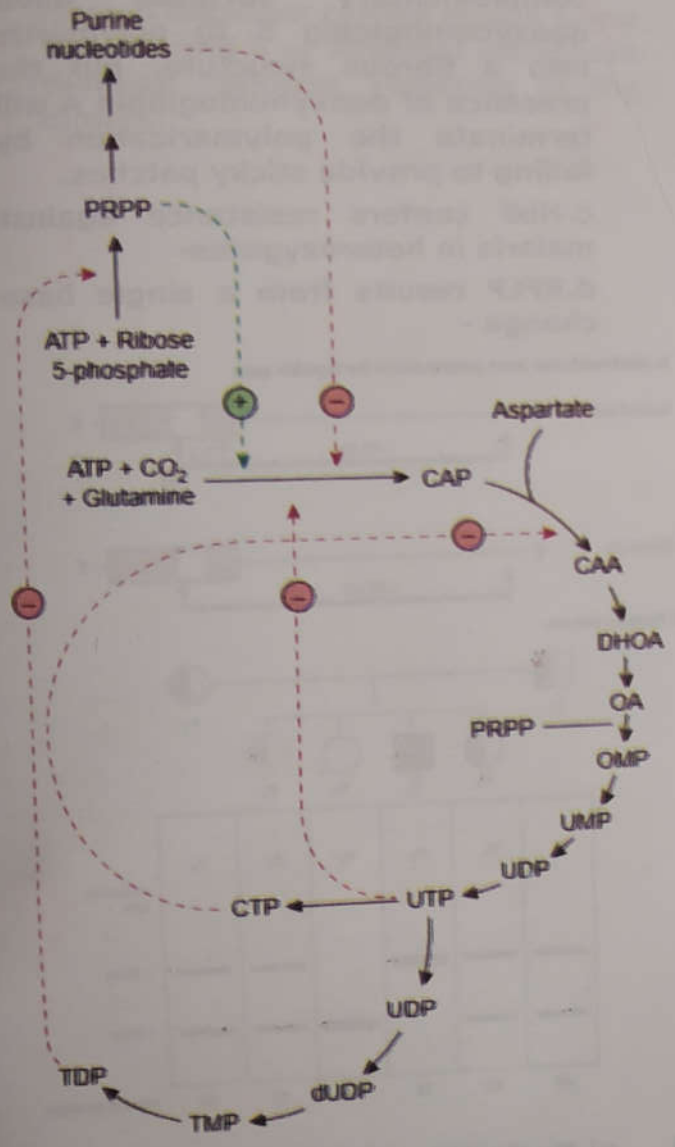
Translation: Synthesis of protein using mRNA as template.

Frameshift Mutations Result from Deletion or Insertion of Nucleotides in DNA That Generates Altered mRNAs The deletion of a single nucleotide from the coding strand of a gene results in an altered reading frame in the mRNA. The machinery translating the mRNA does not recognize that a base was missing, since there is no punctuation in the reading of codons. Thus, a major alteration in the sequence of polymerized amino acids. Altering the reading frame results in a garbled translation of the mRNA distal to the single nucleotide deletion. Not only is the sequence of amino acids distal to this deletion garbled, but reading of the message can also result in the appearance of a nonsense codon and thus the production of a polypeptide both garbled and prematurely terminated . **Insertions of one or two or nonmultiples of three nucleotides into a gene result in an mRNA in which the reading frame is distorted upon translation, and the same effects that occur with deletions are reflected in the mRNA translation. This may result in garbled amino acid sequences distal to the insertion and the generation of a nonsense codon at or distal to the insertion, or perhaps reading through the normal termination codon. Following a deletion in a gene, an insertion (or vice versa) can reestablish the proper reading frame.**

83. b) Carbamoyl phosphate synthetase II
c) Aspartate transcarbomylase

[Ref: Harper's Illustrated biochemistry, 29th Edition]

Gene Expression & Enzyme Activity Both Are Regulated The activities of the first and second enzymes of pyrimidine nucleotide biosynthesis are controlled by allosteric regulation. Carbamoyl phosphate synthase II (reaction, 1 is inhibited by UTP and purine nucleotides but activated by PRPP. Aspartate transcarbamoylase (reaction 2,) is inhibited by CTP but activated by ATP. In addition, the first three and the last two enzymes of the pathway are regulated by coordinate repression and derepression.

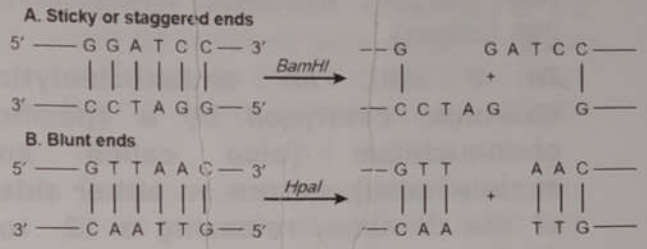


84. b) Allopurinol

The purine analog allopurinol resembles hypoxanthine, used in treatment of hyperuricemia and gout, inhibits purine biosynthesis and xanthine oxidase activity.

85. d) They cleave both strands in duplex DNA

[Ref: Harper's Illustrated biochemistry, 29th Edition]



Results of restriction endonuclease digestion. Digestion with a restriction endonuclease can result in the formation of DNA fragments with sticky, or cohesive, ends (A) or blunt ends (B). This is an important consideration in devising cloning strategies.

Certain endonucleases—enzymes that cut DNA at specific DNA sequences within the molecule (as opposed to exonucleases, which digest from the ends of DNA molecules)—are a key tool in recombinant DNA research. These enzymes were called restriction enzymes because their presence in a given bacterium restricted the growth of certain bacterial viruses called bacteriophages.

86. e) Complete collection of gene copies of one organism

[Ref: Harper's Illustrated biochemistry, 29th Edition]

A Library Is a Collection of Recombinant Clones :

The combination of restriction enzymes and various cloning vectors allows the entire genome of an organism to be individually packed into a vector. A collection of these different recombinant clones is called a library. A genomic library is prepared from the total DNA of a cell line or tissue. A cDNA library comprises complementary DNA copies of the population of mRNAs in a tissue. Genomic DNA libraries are often prepared by performing partial digestion of total DNA with a restriction enzyme that cuts

DNA frequently (eg, a four base cutter such as TaqI).

87. b) DNA ligase

[Ref: Harper's Illustrated biochemistry, 29th Edition]

In E coli, an endonucleolytic cleavage, catalyzed by a specific endonuclease (also called an excinuclease), occurs on either side of the damage, releasing a 12- to 13-base-pair oligonucleotide. The polymerization step involves DNA polymerase and the final step is sealing by DNA ligase.

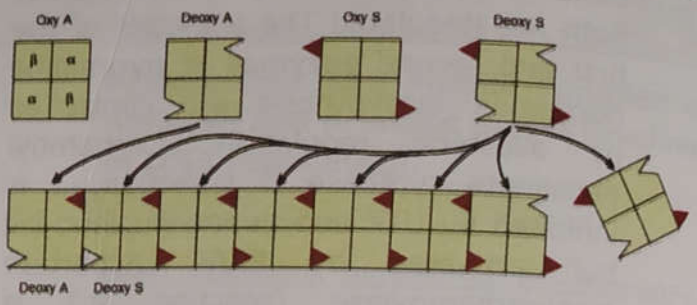
88. b) Sticky patch is generated as a result of replacement of a non polar residue with a polar residue

[Ref: Harper's Illustrated biochemistry, 29th Edition]

a. Single nucleotide change results in change of Glutamine to Valine-

Partially Acceptable Missense Mutations A partially acceptable missense mutation is best exemplified by hemoglobin S, which is found in sickle cell anemia. Here glutamic acid, the normal amino acid in position 6 of the β chain, has been replaced by valine. The corresponding single nucleotide change within the codon would be GAA or GAG of glutamic acid to GUA or GUG of valine. Clearly, this missense mutation hinders normal function since it results in sickle cell anemia when the mutant gene is present in the homozygous state. The glutamate-to-valine change may be considered to be partially acceptable because hemoglobin S does bind and release oxygen, albeit abnormally.

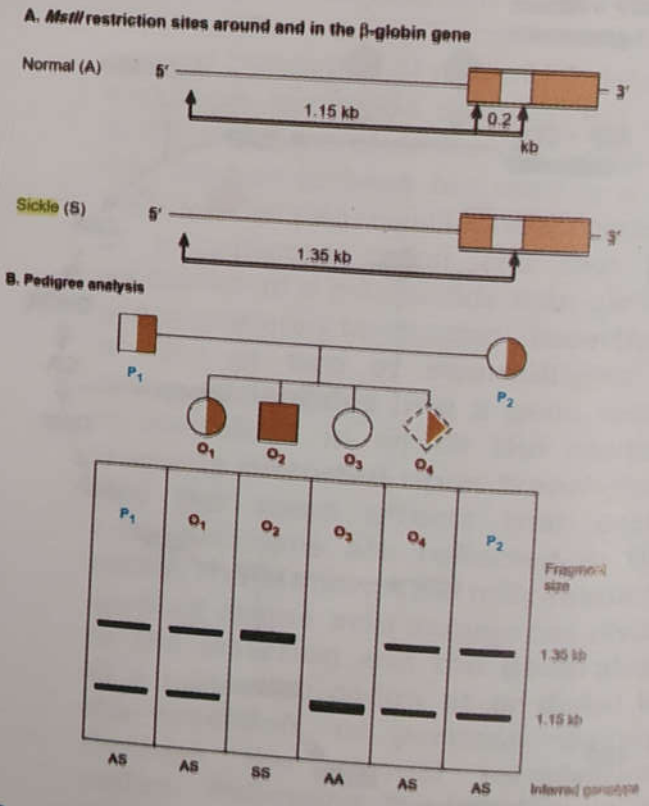
b. Sticky patch is generated as a result of replacement of a non polar residue with a polar residue-



Representation of the sticky patch (Δ) on hemoglobin S and its "receptor" (Δ) on deoxyhemoglobin A and deoxyhemoglobin S. The complementary surfaces allow deoxyhemoglobin S to polymerize into a fibrous structure, but the presence of deoxyhemoglobin A will terminate the polymerization by failing to provide sticky patches.

c. HbS confers resistance against malaria in heterozygotes-

d. RFLP results from a single base change -



89. c) Nucleotide excision repair

[Ref: Harper's Illustrated biochemistry, 29th Edition]

XP is a rare autosomal recessive condition in which the mechanisms for repair of DNA subsequent to damage by UV irradiation are defective. This arises because of mutations in the genes encoding components of the nucleotide excision pathway of DNA repair (nucleotide excision repair, NER). The major damage inflicted on DNA by UV irradiation is the formation of thymine (pyrimidine) dimers (also known as cyclobutane pyrimidine dimers), where covalent bonds are formed between carbon atoms 5 and 5 and 6 and 6 of adjacent intrachain thymine residues, resulting in the dimers.

Exposure to UV light causes formation of thymine dimers in skin cells

↓

Deficient activity of ADA

Thymine dimers are not excised or not correctly repaired because of mutations in the genes encoding components of the nucleotide excision repair pathway

↓

Damage to DNA persists; replication leads to synthesis of DNA containing mutations

↓

Mutant DNA mediates carcinogenesis (possibly by activating oncogenes or inactivating tumor suppressor genes)

↓

Multiple skin tumors may result

Proteins – Questions

Q1. Function of Golgi apparatus:

a. Sorting and packing of proteins
b. Breaking of fatty acids
c. Steroid synthesis
d. DNA replication

Q2. True regarding metabolic acidosis:

a. Body shunts more glutamine from liver to kidneys
b. Less ammonia is excreted in urine
c. Urea synthesis is increased
d. Liver glutaminase activity increases

Q3. In a reaction substrate is available in a concentration that is 1000 times the Km value of the enzyme. After 9 minutes of reaction, 1% substrate is converted to product (12 microgram/ml). If the concentration of the enzyme is changed to 1/3 and concentration of substrate is doubled. What is the time taken to convert the substrate into the same amount of product, i.e. 12 microgram/ml?

a. 9 minutes
b. 4.5 minutes
c. 27 minutes
d. 13.5 minutes

Q4. Hyperphenylalaninemia occurs due to:

a. Phenylalanine hydroxylase deficiency
b. Phenylalanine hydroxylase overactivity
c. Dihydrobiopterin reductase deficiency
d. Tyrosine hydroxylase deficiency
e. Defect in dihydrobiopterin biosynthesis

Q5. Amino acids containing hydroxyl group:

a. Threonine
b. Tyrosine
c. Serine
d. Tryptophan
e. Valine

Q6. During vigorous exercise,which of the following is released from the muscles?

a. Alanine
b. Glutamine
c. Branched keto acid
d. Asparagine

Q7. A patient was loaded with radiolabelled alanine. The patient was scanned after some time. But only radiolabelled glucose was found. Here before forming glucose what does alanine form?

a. Alpha keto glutarate
b. Oxaloacetate
c. Malate
d. L citrulline

Q8. A 60-years-old lady is concerned about her wrinkles around her eyes. This is due to defect in:

a. Fibrillin
b. Collagenase
c. Collagen cross linking
d. Desmosine

Q9. A child died of stroke. Pathological autopsy revealed arterial thromboses. What would you have given in diet to the child to alter his prognosis?

a. Methionine
b. Tyrosine
c. Pyridoxine
d. Thiamine

Q10. An infant presented to the OPD with a history of vomiting and malnutrition. On investigation the Guthrie test was found to be positive. All are true regarding this disease except:

a. Due to PAH enzyme defect
b. White patch of hair due to tryptophan deficiency
c. Phenyl acetate positive in urine
d. Mental retardation is present

Q11. Best method to measure HbA1c?

a. Isoelectric focusing
b. Affinity chromatography
c. Ion exchange chromatography
d. Electrophoresis

1. a	2. a	3. c	4. a, c, e	5. a, b, c	6. a	7. b	8. c
9. c	10. b	11. c					

Q12. Which of the following is NOT a hemeprotein?

a. Myoglobin
b. Cytochrome c
c. Catalase
d. Albumin

Q13. Keratin in skin is softer than keratin in nail because keratin in skin has:

a. Less number of disulphide bonds
b. Less number of salt bridges
c. High sodium content
d. Different affinity for water

Q14. All are true about fibrous proteins except:

a. They have mainly structural functions
b. They have an axial ratio of < 3
c. Elastin is a fibrous protein
d. They have negligible water solubility

Q15. Which one of the following is a feature of homocystinuria?

a. A high incidence of renal calculi
b. An association with dissecting aortic aneurysms
c. Upward dislocation of the lens
d. Elevated plasma methionine levels

Q16. Transmembrane region of a protein is likely to have

a. A stretch of hydrophilic amino acids
b. A stretch of hydrophobic amino acids
c. A disulphide loop
d. Alternating hydrophilic and hydrophobic amino acids

Q17. Select the wrong statement-

a. Bilirubin is a cyclic tetrapyrrole
b. Albumin bound bilirubin is transported to the liver
c. Bilirubin contain methyl and vinyl groups
d. Bilirubin does not contain iron

Q18. Which of the following urea cycle enzymes is/are found in cytosol:

a. Carbamoyl phosphate synthetase I
b. Ornithine transcarbomylase
c. Arginosuccinate synthetase
d. Arginosuccinate lyase
e. Arginase

Q19. Which of the following is/are feature (s) of homocystinuria:

a. Cystine stone formation in kidney
b. Mental retardation
c. Autosomal dominant inheritance
d. Ectopia lentis

Q20. Negative nitrogen balance is seen in all except:

a. Pregnancy
b. TB
c. Protein energy malnutrition
d. Starvation

Q21. Level of protein that remains intact during denaturation:

a. Primary structure
b. Secondary structure
c. Tertiary structure
d. Quaternary structure

Q22. The enzyme which removes hydrogen by adding oxygen is called as:

a. Oxygenase
b. Dehydrogenase
c. Oxidase
d. Reductase

Q23. Enzyme replacement therapy is available for

a. Gauchers disease
b. Galactosemia
c. Fructosuria
d. None

Q24. Enzyme diagnostic of MI in a case of hypothyroidism is

a. SGOT
b. LDH
c. ALDOLASE
d. CPK-MB

Q25. In Competitive inhibition

a. Vmax unchanged
b. Apparent Km unchanged
c. Apparent Km decreased
d. Vmax decreased
e. Rate independent of substrate concentration

Q26. Which of the following is a synthetic reaction?

a. Reduction
b. Acetylation
c. Oxidation
d. Hydrolysis

Q27. Which of the following enzyme is stable at acidic pH?

a. Pepsin
b. Trypsin
c. Chymotrypsin
d. Carboxypeptidase

12. d	13. a	14. b	15. d	16. b	17. a	18. c, d, e	19. b, d
20. a	21. a	22. c	23. a	24. d	25. a	26.b	27. a

Q28. Non- functional enzymes are all except
a. Alkaline phosphatase
b. Acid Phosphatase
c. Lipoprotein lipase
d. Gamma glutamyl transpeptidase

Q29. Serine proteases:
a. Hyrdrolyze peptide bonds involving carboxyl groups of serine resiues
b. Are characterized by having several active sites per molecules, each containing a serine resiue
c. Are inactivate by reaching with one molecule of disopropyl-fluorophosphate per molecules of protein
d. Are exopeptidases

Q30. A non – competitive inhibitor of an enzyme
a. Increases with no little changes in V max
b. Decreases Km
c. Decreases V max
d. Increases Vmax

Q31. Enzyme responsible for respiratory burst is
a. Oxidase
b. Dehydrogenase
c. Peroxidase
d. Catalase

Q32. Km of an enzyme is
a. Dissociation constant
b. The normal physiological substrate concentration
c. The substrate concentration at half maximum velocity
d. Numerically identical for all isoenzymes that catalyze a given reaction

Q33. Isoenzyme
a. Substance to which enzyme acts
b. Physically, distint forms of same enzyme activity
c. Protein pao-crfenzyme
d. Non-protein part of enzyme

Q34. Sarcosine is
a. Glycine
b. N-methylglycine
c. Di-methylglycine
d. Tri-methylglycine

Q35. Most catalytically active enzyme is
a. Trypsin
b. Chymotrypsin
c. Pepsin
d. Galactase

Q36. Kinases require
a. Epinephrine
b. EDTA
c. Inorganic phosphate
d. Mg++
e. Mn

Q37. Enzymes act by
a. Increase in activation energy
b. Decrease in activation energy
c. Shift equilibrium constant

Q38. Glutamine synthetase is a
a. Isomerase
b. Ligase
c. Lyase
d. Transferase

Q39. Carboxylases requires
a. Vitamin B_{12}
b. Folic acid
c. Niacin 12
d. Biotin

Q40. The predominant isoenzyme of LDH occurring in liver injury is
a. LDH-1
b. LDH-2
c. LDH-4
d. LDH-5

Q41. In Xanthine oxidase cofactor is
a. Selenium
b. Zn
c. Molybdenum
d. Mg

Q42. Glutathione peroxidase is a/an
a. Catalase
b. Antioxidant
c. Microsomal enzyme
d. None

Q43. Apoenzyme is
a. Cofactor
b. Coenzyme
c. Protein moiety
d. None

Q44. Type of inhibition of aconitase by Transaconitase is
a. Non – Competitive
b. Competitive
c. Allosteric
d. None

Q45. Action of metalloproteinase
a. Degradation of collagen
b. Polymerization of collagen
c. Oxidation of Collagen
d. Stimulation of Collagen

28. c	29. b	30. c	31. a	32. c	33. b	34. b	35. a	36. d	37. b
38. b	39. d	40. d	41. c	42. b	43.c	44. b	45. a		

Q46. Osteogenesis imperfecta is due to defect in collagen type:

a. 1 b. 2
c. 3 d. 4

Q47. Keratin is chemically :

a. Leucine
b. Cystine
c. Lithium
d. None of the above

Q48. Trace element in carbonic anhydrase is:

a. Copper b. Molybdenum
c. Zinc d. Magnesium

Q49. A signal peptide of collagen is directed from cytoplasms to:

a. Nucleus
b. Golgi bodies
c. Lysosomes
d. Endoplasmic retinaculum

Q50. Which is not an endopeptidase:

a. Trypsin b. Pectin
c. Chymotrypsin d. Aminopeptidase

Q51. Nitric oxide synthase:

a. Is inhibited by Ca++
b. Catalyzes a dioxygenase reaction
c. Accepts electrons from NADH
d. Requires NADH, FAD, FMN & Heme iron

Q52. Enzyme which is a marker of mitochondria is:

a. Glutamate dehydrogenase
b. Acid phosphatase
c. Alkaline phosphatase
d. Hexokinase

Q53. Peroxidase enzyme is used in estimating:

a. Haemoglobin b. Ammonia
c. Creatinine d. Glucose

Q54. All of the above following are trypsin inhibitors, Except

a. Alpha – 1 antitrypsin
b. Alpha- 1 – antiproteinase
c. Enterokinase
d. Egg – white

Q55. Collagen is unique in that it contains much –

a. Cystine b. Cysteine
c. Hydroxyproline d. Glycine
e. Desmossine

Q56. The most abundant protein in the human body is –

a. Myosin b. Albumin
c. Hemoglobin d. Collagen
e. Keratin

Q57. Quaternary structre of protein is –

a. The arrangement sequence of amino acids in the polypeptide chain
b. Inter relation between amino acids in a single polypeptide chain
c. Inter relation and arrangement of polypeptides in a protein with more than 2 polypetide chain
d. None

Q58. True about naturally occurring amino acids is

a. All are racemic mixtures
b. Have specific genetic code
c. All are D isomers
d. All are L isomers

Q59. Which of the following amino acids is purely ketogenic?

a. Lysine b. Arginine
c. Leucine d. Methionine

Leucine –is purely Ketogenic.

Q60. Protein is purified using ammonium sulfate by

a. Salting out
b. Ion exchange chromatography
c. Mass chromatography
d. Molecular size exclusion

Q61. The physiologically important anion other than chloride is

a. Nitrate b. Phosphate
c. Bicarbonate d. Sulphate

Q62. During standard plasma electrophoresis, a protein that moves ahead of albumin is

a. Fibrinogen
b. Alpha feta protein
c. Haemopexin
d. Retinol binding protein

46. a	47. b	48. c	49. d	50. d	51. d	52. a	53. d	54. c	55. c,d
56. d	57. c	58. b	59. c	60. a	61. c	62. d			

Q63. Separation of proteins by their mass
a. Electrophoresis
b. Salting out
c. SDS-PAGE
d. Ion exchange chromatography

Q64. Protein synthesis is sorted out at/ by
a. Ribosomes
b. Mitochondria
c. Golgi apparatus
d. Endoplasmic reticulum

Q65. Ubiquitin breaks down proteins in
a. Lysosomes b. Proteasomes
c. Macrophages d. None

Q66. Change of valine to which amino acid leads to no change in function
a. Lysine b. Praline
c. Leucine d. Tyrosine

Q67. Amino acids with its pKa value within physiologial range is
a. Glycine b. Histidine
c. Lysine d. Arginine

Q68. Quantity of Hb catabolised every day in a normal adult
a. 8 gm b. 10 gm
c. 12 gm d. 13.3 gm

Q69. In sickle cell anemia, glutamine in beta chain is replaced by
a. Arginine b. Alanine
c. Valine d. Methionine

Q70. Glutathione hydrolyzed produce which of the following
a. Glycine b. Cystine
c. Glutamate d. Anserine

Q71. Sulphar containing amino acids are
a. Cystein
b. Asparagine
c. A and B of the above
d. Methionine
e. Glycine

Q72. The semi-essential amino acids are
a. Phenylalanine b. Lysine
c. Tryptophan d. Arginine
e. Histidine

Q73. Chaperones are
a. Mediators of the post-translational assembly of protein complexes
b. Antigen presenting cells
c. Purine metabolism mediators
d. None of the above

Q74. Taurine is biosynthesized by
a. Arginine b. Leucine
c. Valine d. Cysteine

Q75. Carnosine is major constituent of
a. Kidney b. Muscle
c. Brain d. Adipose tissue

Q76. Which is 21st amino acid
a. Alanine b. Cystine
c. Arginine d. Selenocysteine

Q77. Amino acids used for synthesis of Creatine include all EXCEPT
a. Glycine b. Arginine
c. Alanine d. Methionine

Q78. Cystine is formed by
a. Hydroxylation of cysteine molecule
b. Carboxylation of cysteine molecule
c. Peptide bond between two cysteine moleaile
d. Disulfide bond between cysteine molecule

Q79. Ion exchange chromatography is based on
a. Size b. Charge
c. Solubility d. Polarity

Q80. Source of nitrogen in urea cycle is
a. Glutamate and aspartate
b. Glutamate and NH3
c. Arginine and aspartate
d. NH3 and aspartate

Q81. Bence Jones proteins are
a. Light chains
b. Heavy chains
c. Cryoglobulins
d. C- reactive protein

Q82. FIGLU is an intermediate product of
a. Histidine b. Arginine
c. Cystine d. Methionine

63. c	64. c	65. b	66.c	67. b	68. a	69. c	70. a,c	71. a,d	72. d,e
73. a	74. d	75. b	76. d	77. c	78. d	79. b	80. d	81. a	82. a

Q83. Aggrecan are

a. Meant for platelet aggregation
b. For adhesion of cells to basement membrane
c. For adhesion of fibrinogen neceptors to plates
d. Proteoglycan found in cartilage

Q84. Amino acid carrying ammonia from muscle to liver

a. Alanine b. Glutamine
c. Arginine d. Lysine

Q85. Amino acid which does not participate in alpha-helix formation is-

a. Leucine b. Glycine
c. Proline d. Lysine

Q86. Electrophoresis done under pH gradient is-

a. Isoosmotic b. Isoelectectric
c. Ion exchange d. None

Q87. Molecular sepration of two proteins with same charge can be done by –

a. Ion exchange chromatography
b. Djalysis
c. Gel diffusion chromatography
d. Electrophoresis

Q88. Proteins are separated on the basis of size by –

a. SDS – PAGE
b. HPLC
c. Affinity Chromatography
d. Ion – exchange Chromatography

Q89. The structural protein are involved in maintaining the shape of a cell or in the formation of matrix in the body. The shape of these protein is :

a. Globular
b. Fibrous
c. Stretch of beads
d. Planar

Q90. Branched chain ketoacid decarboxylation is defective in:

a. Maple syrup urine disease
b. Hartnup disease
c. Alkatonuria
d. GM1 gangliosiodosis

Q91. Melatonin is synthesized form:

a. Tryphophan b. Serotomin
c. Phenyllanine d. Histidine
e. Leucine

Q92. Amino acid excreted in the urine in cystinosis:

a. Cystine b. Ornithine
c. Arginine d. Lysine
e. All of the above

Q93. In hartnup's disease..... is excreted in the urine:

a. OrNIthine
b. Glycine
c. Tryptophan
d. Phenylalamnine
e. Cystine

83. d	84. a	85. c	86. b	87. c	88. a	89. b	90. a	91. a	92. e
93. c,d									

Proteins – Explanations

1. a) Sorting and packing of proteins

Ref: Harper's Illustrated biochemistry, 29th edition

Structure	Function
Golgi apparatus	• Processing, distribution of proteins and lipids • Major collection and dispatch station of protein products received from the endoplasmic reticulum • Post-translational modification of proteins

2. a) Body shunts more glutamine from liver to kidneys

Ref: Harper's Illustrated Biochemistry, 29th edition

Explanation:

Changes in Glutamine Metabolism in Metabolic Acidosis

- Glutamine metabolism plays a crucial role in body's ability in tackling acidosis
- Glutamine synthesis in Liver is increased
- Ammonia secretion increases
- Metabolism of Glutamine in kidneys produces alpha-ketoglutarate which in turn is decarboxylated, producing Bicarbonate. This bicarbonate enters blood stream and helps to buffer the acid load.
- There is increased processing of glutamine in kidneys.
- Not all the excess NH4+ produced is related into blood stream or converted into urea.
- Bicarbonate produced by the decarboxylation of alpha-ketoglutarate in Krebs cycle also serves as buffer in blood.

Also Note:

Glutamine synthase converts NH3 to nontoxic glutamine.

Glutaminase releases NH3 for use in urea synthesis.

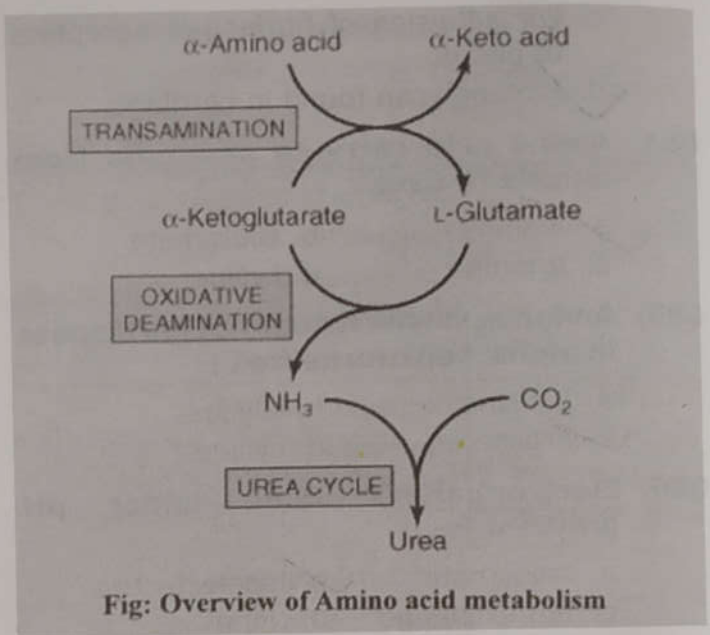


Fig: Overview of Amino acid metabolism

3. c) 27 minutes

[Ref: Lippincott's illustrated reviews, 6th Edition]

During derivation of Michaelis-Menten equation

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P$$

$$V_0 = \frac{k_2[E_t][S]}{K_m + [S]}$$

This equation can be further simplified. Because the maximum velocity occurs when the enzyme is saturated (that is, with [ES] [Et]) V_{max} can be defined as $k_2[Et]$.

$$V_0 = \frac{V_{max}[S]}{K_m + [S]}$$

$$\text{So, } V_{max} = K_2[Et]$$

If total enzyme concentration is reduced by 1/3 and [S] is very high then V_{max} also become 1/3

So in this question same amount of product will be formed in 27 minutes (3 x 9 min)

4. **a) Phenylalanine hydroxylase deficiency**
c) Dihydrobiopterin reductase deficiency
e) Defect in dihydrobiopterin biosynthesis

[Ref: Harper's Illustrated biochemistry, 30th Edition & Lippincott's illustrated reviews, 6th Edition]

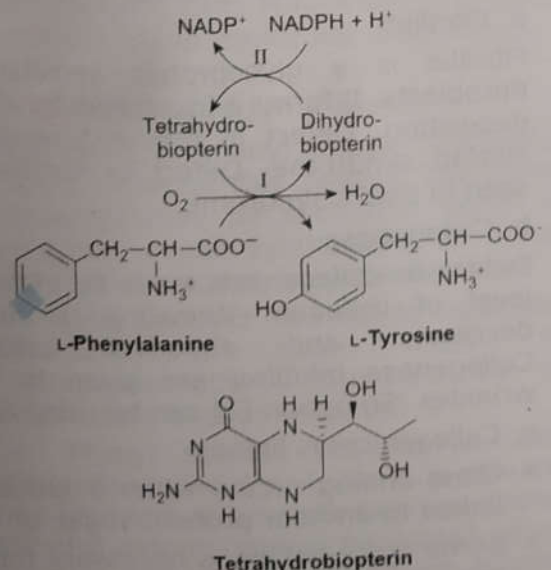
a. Phenylalanine hydroxylase deficiency –

Phenylalanine

Phenylalanine is first converted to tyrosine. Subsequent reactions are those of tyrosine

- Hyperphenylalaninemias arise from defects in phenylalanine hydroxylase itself (type I, classic phenylketonuria or PKU), in dihydrobiopterin reductase (types II and III), or in dihydrobiopterin biosynthesis (types IV and V) . Alternative catabolites are excreted.

A diet low in phenylalanine can prevent the mental retardation of PKU. DNA probes facilitate prenatal diagnosis of defects in phenylalanine hydroxylase or dihydrobiopterin reductase. Elevated blood phenylalanine may not be detectable until 3-4 days postpartum. False-positives in premature infants may reflect delayed maturation of enzymes of phenylalanine catabolism.



Synthesis of tyrosine from phenylalanine

The phenylalanine hydroxylase reaction. Two distinct enzymatic activities are involved. Activity II catalyzes reduction of dihydrobiopterin by NADPH, and activity I the reduction of O2 to H2O and of phenylalanine to tyrosine. This reaction is associated with several defects of phenylalanine metabolism .

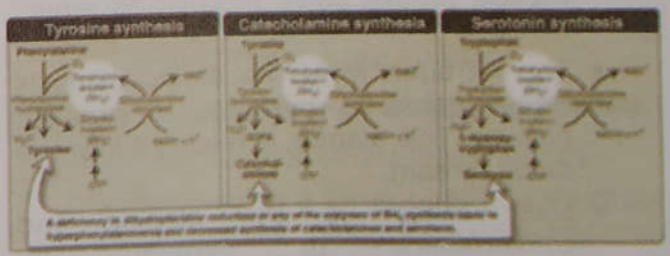
b. Phenylalanine hydroxylase overactivity-

Cannot cause phenylketonuria.

c. Dihydrobiopterin reductase deficiency –

Phenylketonuria (PKU)

- PKU is caused by a deficiency of phenylalanine hydroxylase, is the most common clinically encountered inborn error of amino acid metabolism
- Biochemically, it is characterized by accumulation of phenylalanine (and a deficiency of tyrosine).
- Such deficiencies indirectly raise phenylalanine concentrations, because phenyl alanine hydroxylase requires BH_4 as a coenzyme. BH_4 is also required for tyrosine hydroxylase and tryptophan hydroxylase, which catalyze reactions leading to the synthesis of neurotransmitters, such as serotonin and reverse the central nervous system (CNS) effects due to deficiencies in neurotransmitters.



Biosynthetic reactions involving amino acids and tetrahydrobiopterin

d. Tyrosine hydroxylase deficiency –

"Tyrosine Hydroxylase (TH) deficiency (also known as Recessive Dopa - Responsive Dystonia) is a rare metabolic disorder characterized by the lack of the enzyme involved in converting the amino acid tyrosine to L-dopa. TH is a critical enzyme in normal dopamine production" -

e. Defect in dihydrobiopterin biosynthesis

Hyper phenyl alaninemia may also be

caused by deficiencies in any of the several enzymes required to synthesize BH4, or in dihydropteridine reductase, which regenerates BH_4 from BH2.

5. a) Threonine
b) Tyrosine
c) Serine

[Ref: Lippincott's illustrated reviews, 6th Edition]

a. Threonine-

"Serine, threonine, and tyrosine each contain a polar hydroxyl group than can participate in hydrogen bond formation. The side chains of asparagine and glutamine each contain a carbonyl group and an amide group, both of which can also participate in hydrogen bonds"-Lippincott 6th/4

b. Tyrosine-have hydroxyl group

c. Serine- have hydroxyl group

d. Tryptophan-does not have hydroxyl group

e. Valine-does not have hydroxyl group

6. a) Alanine

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Alanine-

Glucose-alanine cycle happens during fasting. It Is also seen in vigorous exercise.

- During fasting or strenuous exercise, muscle breaks down proteins to amino acids.
- The nitrogen from the amino acids is transminated to pyruvate to produce alanine. This alanine is released into the blood stream.
- Liver takes up the alanine and convertsback to pyruvate by transamination.
- Pyruvate Is glucogenic.

Biochemical changes seen in vigorous exercise are:

- ↑CK-MB, AST, ALT in plasma.
- ↓ Na^+, K^+, Glucose plasma.
- Proteinuria.

b. Glutamine –

Glutamine helps in ammonia detoxification from brain.

c. Branched keto acid –

Branched keto acids are excreted in Maple syrup urine disease.

d. Asparagine –

Asparagine is a non-essential amino acid that can be synthesised from aspartate.

7. b) Oxaloacetate

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Since the question mentions radio labelled glucose is found. So we should just trace the pathway of conversion of alanine to glucose.

a. Alpha keto glutarate-

During transamination, α ketoglutarate accepts the amino group of alanine. In TCA cycle,it is produced from isocitrate dehydrogenase. The question is about gluconeogenesis hence Alpha keto glutarate is excluded.

b. Oxaloacetate-

Alanine is a glucogenic amino acid. In the liver, it donates its amino group to become pyruvate. As pyruvate is not given in the option, we have to trace the pathway more. Pyruvate is carboxylated to oxaloacetate by pyruvate carboxylase. So, the answer is oxaloacetate.

c. Malate- is produced in TCA cycle hence excluded.

d. L citrulline-is produced in urea cycle hence excluded.

8. c) Collagen cross linking

a. Fibrillin-

Fibrillin is a glycoprotein secreted by fibroblasts. It forms a framework for elastin deposition. Defect in fibrillin-1 results in Marfan syndrome. Defect in fibrillin-2 is seen in Beal's syndrome.

b. Collagenase-

Defect in collagenase leads to increased level of collagen. Wrinkling is due to decreased and abnormal collagen. Collagenase inhibitor are given to treat wrinkles. So option (b) can be ruled out.

c. Collagen cross linking-

- Cross-linking occurs when a protein is linked to another protein, sugar, or lipid
- Some cross-linking is necessary for the normal collagen function

- Abnormal cross-linking causes wrinkling/ ages skin.
- Abnormal cross-linking is due to glucose mediated advanced glycation end products (AGE), UV mediated free radical damage.

d. Desmosine-

Desmosine cross-link is present in elastin. It is formed by 3 allysyl side chains plus one unaltered lysyl side chain of elastin

9. c) Pyridoxine

[Ref: Harper's Illustrated biochemistry, 30th Edition]

a. Methionine- Methionine should be restricted; cysteine should be given in diet

b. Tyrosine- Tyrosine becomes essential in phenylketonuria

c. Pyridoxine –

Homocystinuria

- Autosomal recessive disease due to defect in methionine catabolism. Classical homocystinuria is due to cystathionine β synthase deficiency.
- This is of 2 types:
- Pyridoxine responsive.
- Pyridoxine unresponsive.

d. Thiamine- Thiamine is given in beriberi

10. b) White patch of hair due to tryptophan deficiency

[Ref: DM Vasudevan Textbook of Biochemistry for medical student , 7th Edition Devlin's textbook of Biochemistry, 7th Edition & Tietz Fundamental of clinical chemistry and molecular diagnostics, 7th Edition]

a. Due to PAH enzyme defect-

Deficiency of phenyl alanine hydroxylase is the cause for this disease. The genetic mutation may be such that either the enzyme is not synthesized or a non-functional enzyme is synthesized.

b. White patch of hair due to tryptophan deficiency-The child often has hypopigmentation, explained by the decreased level of tyrosine.

c. Phenyl acetate positive in urine- Phenylalanine level in blood is elevated. So alternate minor pathways are opened. Phenyl ketone (phenyl pyruvate), phenyl lactate and phenyl acetate are excreted in urine.

d. Mental retardation is present-The classical PKU child is mentally retarded with an IQ of 50. About 20% inmates of lunatic asylum may have PKU.Agitation, hyperactivity, tremors and convulsions are often manifested. This may be because phenylalanine interferes with neurotransmitter synthesis.

11. c) Ion exchange chromatography

[Ref: Tietz Textbook of clinical chemistry and molecular biology, 5th Edition]

Methods for the Determination of Glycated Haemoglobins:

These methods separate GHb from nonglycated haemoglobin using techniques based on charge differences (ion-exchange chromatography, HPLC, electrophoresis, and isoelectric focusing), structural differences (affinity chromatography and immunoassay), or chemical analysis (photometry and spectrophotometry).

12. d) Albumin

a. Myoglobin- Heme proteins are ubiquitous in biology and serve diverse functions including, but not limited to, oxygen transport and storage (eg, hemoglobin and myoglobin) and electron transport (eg, cytochrome c and cytochrome P450).

b. Cytochrome c-Heme Protein

c. Catalase- Heme Protein

d. Albumin-It is a glycoprotein

13. a) Less number of disulphide bonds

a. Less number of disulphide bonds-

Keratins form a large family, with about 30 members being distinguished. As indicated in Table two major types of keratins are found; all individual keratins are heterodimers made up of one member of each class.

Keratins	Molecular Mass (kDa)	Distribution
Type I (acidic)	40-60	Epithelial cells, hair, nails
Type II (basic) 50-70 As for type I (acidic)	Type II (basic) 50-70 As for type I (acidic)	Type II (basic) 50-70 As for type I (acidic)

b. Less number of salt bridges-keratin does not form salt bridges.

c. High sodium content-Keratin does not have High sodium content

d. Different affinity for water-Keratin of hair and nails have similar affinity for water.

14. b) They have an axial ratio of < 3

a. They have mainly structural functions-Collagen is the most abundant of the fibrous proteins that constitute more than 25% of the protein mass in the human body. Other prominent fibrous proteins include keratin and myosin. These fibrous proteins represent a primary source of structural strength for cells (ie, the cytoskeleton) and tissues. Skin derives its strength and flexibility from an intertwined mesh of collagen and keratin fibers, while bones and teeth are buttressed by an underlying network of collagen fibers analogous to steel strands in reinforced concrete. Collagen also is present in connective tissues such as ligaments and tendons. The high degree of tensile strength required to fulfill these structural roles requires elongated proteins characterized by repetitive amino acid sequences and a regular secondary structure.

b. They have an axial ratio of < 3 - By contrast, many structural proteins adopt highly extended conformations. These fibrous proteins may possess axial ratios of 10 or more.

c. Elastin is a fibrous protein –Elastin is a connective tissue protein that is responsible for properties of extensibility and elastic recoil in tissues..

d. They have negligible water solubility –globular proteins are water soluble as compared to fibrous proteins.

15. d) Elevated plasma methionine levels

a. A high incidence of renal calculi - cystine-lysinuria is associated with renal calculi.

b. An association with dissecting aortic aneurysms - People with elevated serum levels of homocysteine (homocysteinemia) or the disulfide- linked dimer homocystine (homocystinuria) have an unusually high risk for coronary heart disease and arteriosclerosis.

c. Upward dislocation of the lens-Is associated with inward and downward dislocation of lens

d. Elevated plasma methionine levels -

The most common genetic cause of high homocysteine levels is a mutation within the gene encoding cystathionine b- synthase. High levels of homocysteine appear to damage cells lining blood vessels and to increase the growth of vascular smooth muscle. The amino acid raises oxidative stress as well and has also been implicated in the development of type 2 diabetes .The molecular basis of homocysteine's action has not been clearly identified, but may result from stimulation of the inflammatory response. Vitamin treatments are sometimes effective in reducing homocysteine levels in some people. Treatment with vitamins maximizes the activity of the two major metabolic pathways processing homocysteine. Pyridoxal phosphate, a vitamin B 6 derivative, is necessary for the activity of cystathionine b -synthase, which converts homocysteine into cystathione; tetrahydrofolate, as well as vitamin B 12, supports the methylation of homocysteine to methionine.

16. b) A stretch of hydrophobic amino acids

a. A stretch of hydrophilic amino acids – this is present on the outer side.

b. A stretch of hydrophobic amino acids-proteins generally span the bilayer as a bundle of α-helical transmembrane segments. Integral proteins are usually globular and are themselves amphipathic. They consist of two hydrophilic ends separated by an intervening hydrophobic region that traverses the hydrophobic core of the bilayer. As the structures of integral membrane proteins were being elucidated, it became apparent that certain ones (eg, transporter molecules, ion channels, various receptors, and G proteins) span the bilayer many times, whereas other simple membrane proteins (eg, glycophorin A) span the membrane only once.

c. A disulphide loop-it is part of many proteins but not usually present in Transmembrane region.

d. Alternating hydrophilic and hydrophobic amino acids-this is not a characteristic of Transmembrane region.

17. a) Bilirubin is a cyclic tetrapyrrole

a. Bilirubin is a cyclic tetrapyrrole-

The first step in the degradation of the heme group is the cleavage of its alpha- methine bridge to form the green pigment biliverdin, a linear tetrapyrrole. The central methine bridge of biliverdin is then reduced by biliverdin reductase to form bilirubin, a red pigment . The changing color of a bruise is a highly graphic indicator of these degradative reactions.

b. Albumin bound bilirubin is transported to the liver-

Bilirubin Is Transported to the Liver Bound to Serum Albumin:

Bilirubin is only sparingly water-soluble, but bilirubin bound to serum albumin is readily transported to the liver. Albumin appears to have both a high-affinity site and a low-affinity site for bilirubin. The high-affinity site can bind approximately 25 mg of bilirubin/100 mL of plasma. More loosely bound bilirubin can readily be detached and diffuse into tissues, and antibiotics and certain other drugs can compete with and displace bilirubin from albumin's high-affinity site.

c. Bilirubin contain methyl and vinyl groups-

The desaturation of the porphyrin ring and the conversion of two of the propionate side chains into vinyl groups yield protoporphyrin IX.Which have methyl ,vinyl, propionate side chains.

d. Bilirubin does not contain iron-

The chelation of iron finally gives heme, the prosthetic group of proteins such as myoglobin, hemoglobin, catalase, peroxidase, and cytochrome c. The insertion of the ferrous form of iron is catalyzed by ferrochelatase. Iron is transported in the plasma by transferrin, a protein that binds two ferric ions, and is stored in tissues inside molecules of ferritin.

18. c) Arginosuccinate synthetase
d) Arginosuccinate lyase
e) Arginase

High yielding facts

- Carbomyl phosphate synthetase I reaction is rate limiting step in urea formation-Vasudevan 5th/180
- Urea cycle is also k/a Krebs-Henseleit cycle or ornithine cycle- Satya Narayan 4th/337; Vasudevan 5th/180
- Urea has two amino groups, one derived from NH3 and the other from aspartate. Carbon atom is supplied by CO2-Satyanarayan 4th/337
- Urea is synthesized in liver

19. b) Mental retardation
d) Ectopia lentis

[Ref: **Harrison 19th** Edition]

Inherited Disorders of Amino Acid Metabolism (Partial list)

Condition	Enzyme Defect	Clinical Findings
Homocystinuria	Cystathionine β-synthase	Lens dislocation, thrombotic vascular disease, mental retardation, osteoporosis
Homocystinuria	5, 10 - Methylene tetrahy drofolate reductase	Mental retardation, gait and psychiatric abnormalities, recurrent strokes
Homocystinuria	Methionine synthase (cbIE,-G)	Mental retardation, hypotonia, seizures, megaloblastic anemia
Homocystinuria and methylmalonic acidemia	Vitamin B12 lysosomal efflux and metabolism (cbl C,-D, -F)	Mental retardation, lethargy, failure to thrive, hypotonia, seizures, megaloblastic anemia

20. a) Pregnancy

[Ref: Mark's Basic Medical Biochemistry – A Clinical Approach, 4th edition]

Factors Affecting Nitrogen Balance

I. Growth: During the period of active growth, a state of positive nitrogen balance exists. On an average when a person gains 5 kg, about 1 kg proteins are added to the body. For this, about 160 g of nitrogen has to be retained, so he/she has to be positive nitrogen balance.

II. Hormones: Growth hormone, insulin and androgens promote positive nitrogen balance, while corticosteroids cause a negative nitrogen balance.

III. Pregnancy: A pregnant woman will be in a state of positive nitrogen balance due to the growth of fetus.

IV. Convalescence: A person convalescing after an illness or surgery will be in positive nitrogen balance, due to active regeneration of tissues.

V. Acute illness: Negative nitrogen balance is seen in subjects immediately after surgery, trauma and burns.

VI. Chronic illness: malignancy, uncontrolled diabetes mellitus and other debilitating diseases show negative nitrogen balance.

VII. Protein deficiency: The deficiency of even a single essential amino acid can cause negative nitrogen balance. Prolonged starvation is another important cause.

21. a) Primary structure

In Denaturation primary structure remains intact.

22. c) Oxidase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Oxidases use oxygen as a hydrogen acceptor

Oxidases catalyse the removal of hydrogen from a substrate using oxygen as a hydrogen acceptor. They form water or hydrogen peroxide as a reaction product.

23. a) Gauchers disease

The sphingolipidoses (lipid storage diseases) are a group of inherited diseases that are caused by a genetic defect in the catabolism of lipids containing sphingosine. There is no effective treatment for many of the diseases, although some success has been achieved with enzyme replacement therapy and bone marrow transplantation in the treatment of Gaucher's and Fabry's diseases. Other promising approaches are substrate deprivation therapy to inhibit the synthesis of sphingolipids and chemical chaperone therapy. Gene therapy for lysosomal disorders is also currently under investigation.

24. d) CPK-MB

a. SGOT
b. LDH
c. ALDOLASE
d. CPK-MB

Creatine kinase (CK) has three isozymes: CK-MM (skeletal muscle), CK-BB (brain), and CK-MB (heart and skeletal muscle). CK-MB has a useful diagnostic window. It appears within 4–6 h of an MI, peaks at 24 h, and returns to baseline by 48–72 h. As for LDH, individual CK isozymes are separable by electrophoresis, thus facilitating detection. Today, in most clinical laboratories for the diagnosis of MI CK has been supplemented by troponin. However, as CK-MB also is released upon skeletal muscle injury, assay of plasma CK levels continues in use to assess skeletal muscle disorders such as Duchenne muscular dystrophy. Troponin is a complex of three proteins involved in muscle contraction in skeletal and cardiac muscle but not in smooth muscle. Immunological measurement of plasma levels of cardiac troponins I and T provide sensitive and specific indicators of damage to heart muscle. Troponin levels rise 2–6 h after an MI and remain elevated for 4–10 days.

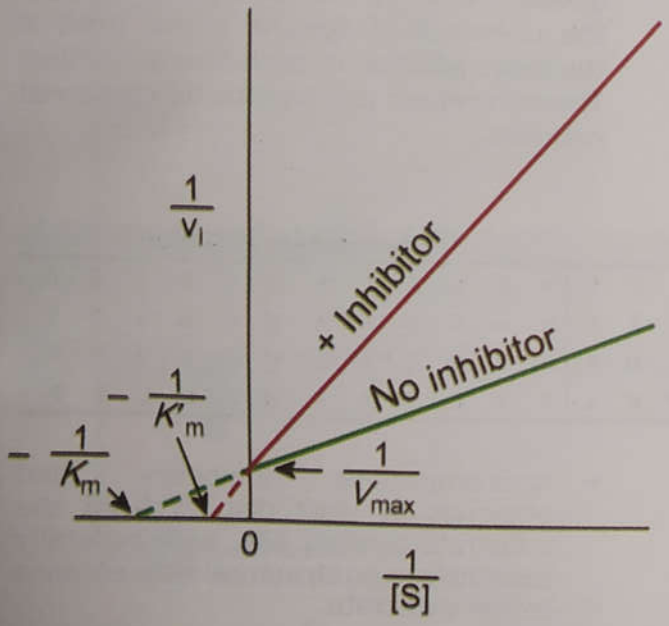
25. a) Vmax unchanged

a. Vmax unchanged
b. Apparent Km unchanged
c. Apparent Km decreased
d. Vmax decreased
e. rate independent of substrate concentration

in Competitive Inhibition:

Since the y intercept is equal to 1/Vmax, this pattern indicates that when 1/[S] approaches 0, vi is independent of the presence of inhibitor. Note, however, that the intercept on the xaxis does vary with inhibitor concentration—and that since −1/K'm is smaller than 1/Km, K'm (the "apparent Km") becomes larger in the presence of increasing concentrations of the inhibitor. Thus, a competitive inhibitor has no effect on Vmax but raises K'm, the apparent Km for the substrate.

Once Km has been determined in the absence of inhibitor, Ki can be calculated . Ki values are used to compare different inhibitors of the same enzyme. The lower the value for Ki, the more effective the inhibitor.



Lineweaver-Burk plot of competitive inhibition. Note the complete relief of inhibition at high [S] (ie, low 1/[S]).

26. b) Acetylation

a. Reduction

b. Acetylation-

Synthetic reactions means to synthesize or to build up.Of all the options provided acetylation reactions directly form the substrate.

c. Oxidation

d. Hydrolysis

27. a) Pepsin

a. Pepsin-

The proteases are secreted as inactive zymogens; the active site of the enzyme is masked by a small region of the peptide chain that is removed by hydrolysis of a specific peptide bond. Pepsinogen is activated to pepsin by gastric acid and by activated pepsin (autocatalysis).

b. Trypsin-

In the small intestine, trypsinogen, the precursor of trypsin, is activated by enteropeptidase, which is secreted by the duodenal epithelial cells; trypsin can then activate chymotrypsinogen to chymotrypsin, proelastase to elastase, procarboxypeptidase to carboxypeptidase, and proaminopeptidase to aminopeptidase.

c. Chymotrypsin-see option b

d. Carboxypeptidase-see option b

28. c) Lipoprotein lipase

a. Alkaline phosphatase

b. Acid Phosphatase

c. Lipoprotein lipase

d. Gamma glutamyl transpeptidase

The analysis of certain enzymes aids diagnosis:

The analysis of enzymes in blood plasma has played a central role in the diagnosis of several disease processes. Many enzymes are functional constituents of blood. Examples include pseudocholinesterase, lipoprotein lipase, and components of the cascade of events in blood clotting and clot dissolution.

Other enzymes are released into plasma following cell death or injury. While these latter enzymes perform no physiologic function in plasma, their appearance or levels can assist in the diagnosis and prognosis of diseases and injuries affecting specific tissues. Following injury, the plasma concentration of a released enzyme may rise early or late, and may decline rapidly or slowly.

Serum Enzyme	Major Diagnostic Use
Aminotransferases	
Aspartate aminotransferase (AST, or SGOT)	Myocardial infarction
Alanine aminotransferase (ALT, or SGPT)	Viral hepatitis

Amylase	Acute pancreatitis
Ceruloplasmin	Hepatolenticular degeneration (Wilson's disease)
Creatine kinase	Muscledisorders and myocardial infarction
γ-Glutamyl transferase	Various liver diseases
Lactate dehydrogenase isozyme 5	Liver diseases
Lipase	Acute pancreatitis
Phosphatase, acid	Metastatic carcinoma of the prostate
Phosphatase, alkaline (isozymes)	Various bone disorders, obstructive liver diseases

29. b) Are characterized by having several active sites per molecules, each containing a serine resiue

a. Hyrdrolyze peptide bonds involving carboxyl groups of serine resiues.

b. Are characterized by having several active sites per molecules, each containing a serine resiue.

Proteases catalyze the hydrolysis of proteins into their component amino acids: Members of an enzyme family such as the aspartic or serine proteases employ a similar mechanism to catalyze a common reaction type but act on different substrates. For example, in chymotrypsin, which cleaves peptide bonds on the carboxyl terminal side of large hydrophobic amino acids, and trypsin, which cleaves peptide bonds on the carboxyl terminal side of basic amino acids. Proteins that diverged from a common ancestor are said to be homologous to one another. The common ancestry of enzymes can be inferred from the presence of specific amino acids in the same position in each family member. These residues are said to be conserved residues.

Enzyme	Sequence Around Serine Ⓢ														Sequence Around Histidine Ⓗ											
Trypsin	D	S	C	Q	D	G	Ⓢ	G	G	P	V	V	C	S	G	K	V	V	S	A	A	Ⓗ	C	Y	K	S	G
Chymotrypsin A	S	S	C	M	G	D	Ⓢ	G	G	P	L	V	C	K	K	N	V	V	T	A	A	Ⓗ	G	G	V	T	T
Chymotrypsin B	S	S	C	M	G	D	Ⓢ	G	G	P	L	V	C	Q	K	N	V	V	T	A	A	Ⓗ	C	G	V	T	T
Thrombin	D	A	C	E	G	D	Ⓢ	G	G	P	F	V	M	K	S	P	V	L	T	A	A	Ⓗ	C	L	L	Y	P

Table illustrates the primary structural conservation of two components of the charge-relay network for several serine proteases. Among the most highly conserved residues are those that participate directly in catalysis.

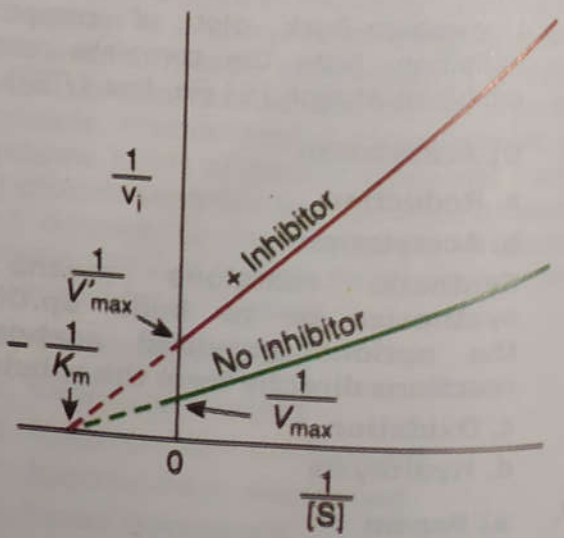
c. Are inactivate by reaching with one molecule of disopropyl-fluorophosphate per molecules of protein

d. Are exopeptidases

30. c) Decreases V max

Simple Noncompetitive Inhibitors Lower Vmax But Do Not Affect Km

- In noncompetitive inhibition, binding of the inhibitor does not affect binding of substrate.
- Formation of both EI and EIS complexes is therefore possible. However, while the enzyme inhibitor complex can still bind substrate, its efficiency at transforming substrate to product, reflected by Vmax, is decreased.
- Noncompetitive inhibitors bind enzymes at sites distinct from the substrate-binding site and generally bear little or no structural resemblance to the substrate.



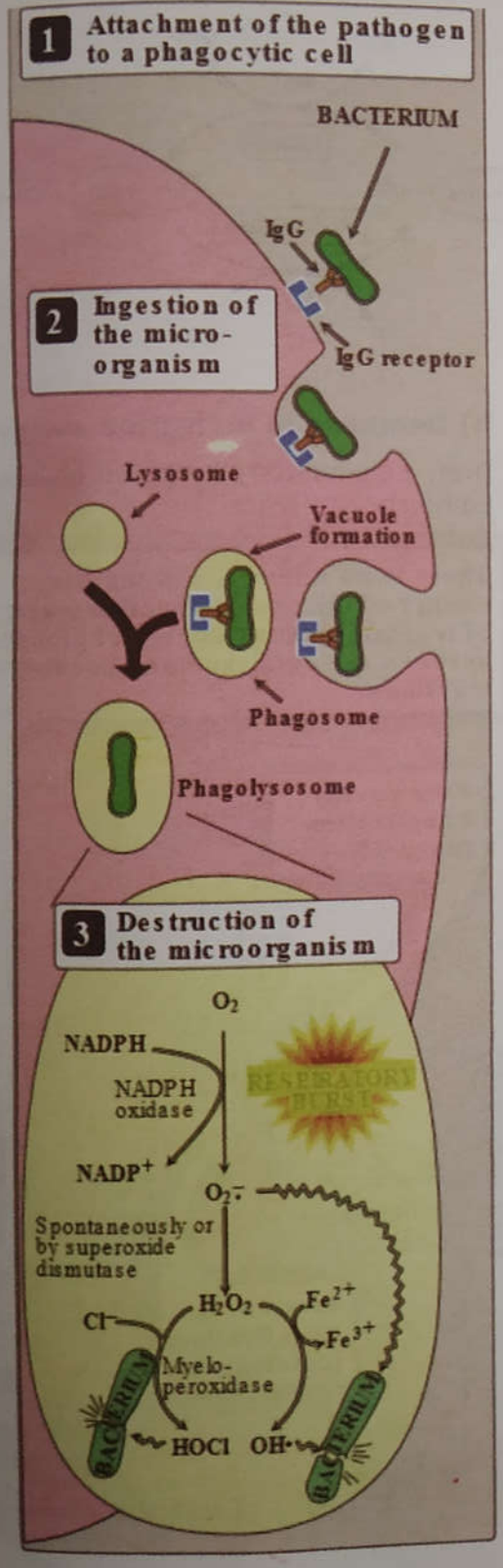
- For simple noncompetitive inhibition, E and EI possess identical affinity

for substrate, and the EIS complex generates product at a negligible rate.

Lineweaver-Burk plot for simple noncompetitive inhibition.

31. a) Oxidase

[Ref: Lippincott's illustrated reviews, 6th Edition]



Oxygen-dependent system:

Oxygen-dependent mechanisms include the enzymes NADPH oxidase and myeloperoxidase (MPO) that work together in killing bacteria . After internalization of the microorganism has occurred, NADPH oxidase, located in the leukocyte cell membrane, is activated and reduces O2 from the surrounding tissue to superoxide (O2 – •), a free radical, as NADPH is oxidized. The rapid consumption of O2 that accompanies formation of O2 – • is referred to as the "respiratory burst." Next, O2 – • is converted to H2O2 (a ROS), either spontaneously or catalyzed by superoxide dismutase. In the presence of MPO, a heme-containing lysosomal enzyme present within the phagolysosome, peroxide plus chloride ions are converted to hypochlorous acid ([HOCl] the major component of household bleach), which kills the bacteria.

32. c) The substrate concentration at half maximum velocity

Km, the Michaelis constant, is characteris tic of an enzyme and its particular substrate and reflects the affin ity of the enzyme for that substrate. Km is numerically equal to the substrate concentration at which the reaction velocity is equal to 1/2Vmax. Km does not vary with enzyme concentration.

a. Small Km: A numerically small (low) Km reflects a high affinity of the enzyme for substrate, because a low concentration of sub strate is needed to halfsaturate the enzyme—that is, to reach a velocity that is 1/2Vmax

b. Large Km: A numerically large (high) Km reflects a low affinity of enzyme for substrate because a high concentration of sub strate is needed to halfsaturate the enzyme.

33. b) Physically, distint forms of same enzyme activity

[Ref: Lippincott's illustrated reviews, 6th Edition]

Isozymes are distinct enzyme forms that catalyze the same reaction

Higher organisms often elaborate several physically distinct versions of a given enzyme, each of which catalyzes the same reaction. Like the members of

other protein families, these protein catalysts or isozymes arise through gene duplication. Isozymes may exhibit subtle differences in properties such as sensitivity to particular regulatory factors or substrate affinity (eg, hexokinase and glucokinase) that adapt them to specific tissues or circumstances. Some isozymes may also enhance survival by providing a "backup" copy of an essential enzyme.

Isoenzymes may contain different numbers of charged amino acids and may, therefore, be separated from each other by electrophoresis.

34. b) N-methylglycine

Sarcosine (N-Methylglycine)

The biosynthesis and catabolism of sarcosine (N-methylglycine) occur in mitochondria. Formation of sarcosine from dimethylglycine is catalyzed by the flavoprotein dimethylglycine dehydrogenase, which requires reduced pteroylpentaglutamate (TPG)

Dimethylglycine + $FADH_2$ + H_4TPG + H_2O → Sarcosine + N-formyl-TPG

35. a) Trypsin

[Ref: Lippincott's illustrated reviews, 6th Edition]

a. Trypsin -

Digestion & absorption of proteins

Few bonds are accessible to the proteolytic enzymes that catalyze hydrolysis of peptide bonds, without prior denaturation of dietary proteins (by heat in cooking and by the action of gastric acid).

Pepsinogen is activated to pepsin by gastric acid and by activated pepsin (autocatalysis). In the small intestine, trypsinogen, the precursor of trypsin, is activated by enteropeptidase, which is secreted by the duodenal epithelial cells; trypsin can then activate chymotrypsinogen to chymotrypsin, proelastase to elastase, procarboxypeptidase to carboxypeptidase, and proamino-peptidase to aminopeptidase.

b. Chymotrypsin

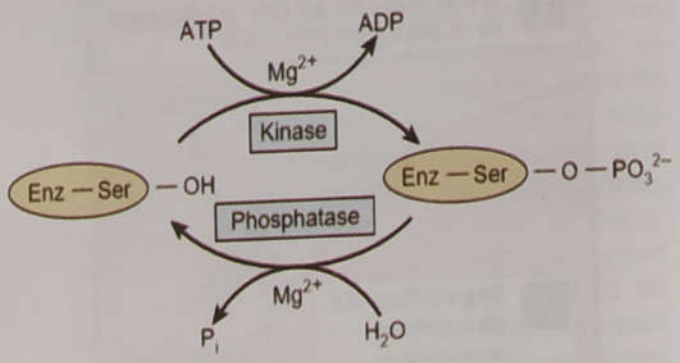
c. Pepsin

d. Galactase

36. d) Mg++

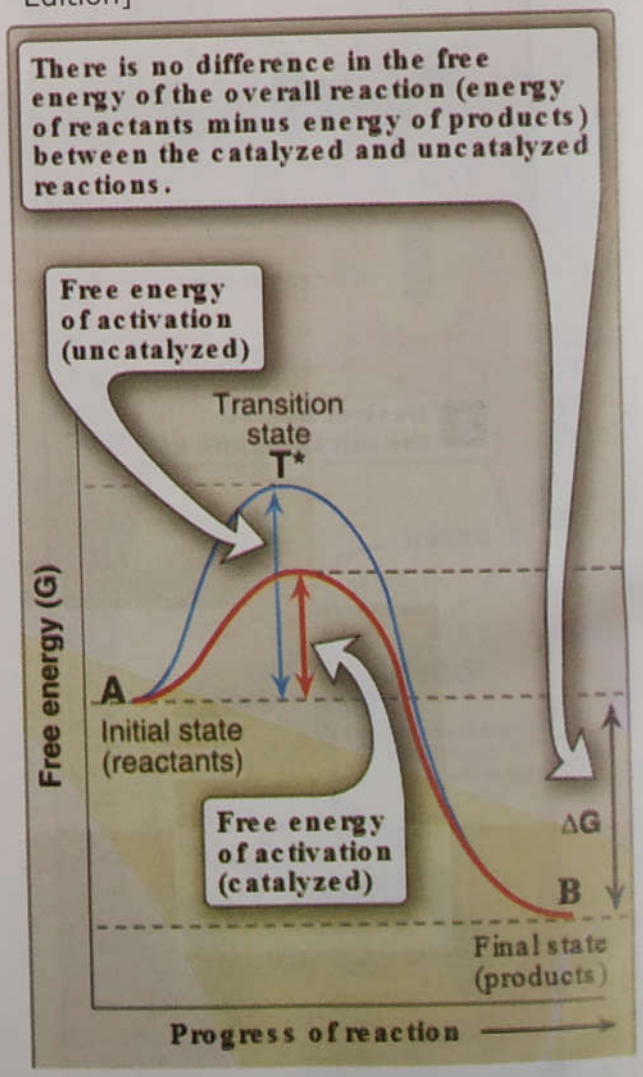
[Ref: Harper's Illustrated biochemistry, 30th Edition]

Protein kinases phosphorylate proteins by catalyzing transfer of the terminal phosphoryl group of ATP to the hydroxyl groups of seryl, threonyl, or tyrosyl residues, forming O-phosphoseryl, O-phosphothreonyl, or O-phosphotyrosyl residues, respectively .



37. b) Decrease in activation energy

[Ref: Lippincott's illustrated reviews, 6th Edition]

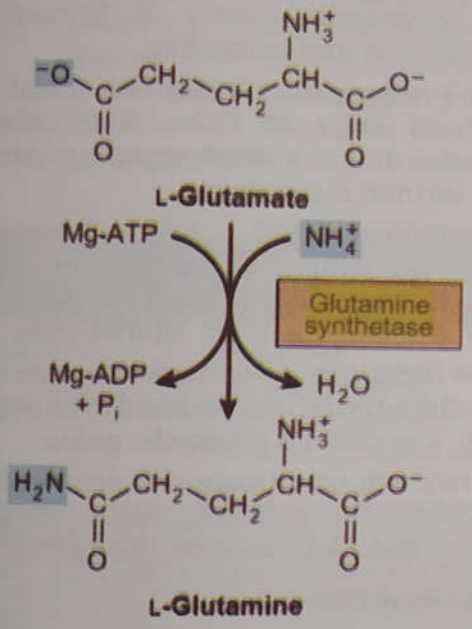

There is no difference in the free energy of the overall reaction (energy of reactants minus energy of products) between the catalyzed and uncatalyzed reactions.
Free energy of activation (uncatalyzed)
Transition state
T*
Free energy (G)
A
Initial state (reactants)
Free energy of activation (catalyzed)
ΔG
B
Final state (products)
Progress of reaction

Free energy of activation: The peak of energy is the difference in free energy between the reactant and T*, where the highenergy intermediate is formed during the conversion of reac tant to product. Because of the high free energy of activation, the rates of uncatalyzed chemical reactions are often slow.

Effect of an enzyme on the activation energy of a reaction.

38. b) Ligase

[Ref: Harper's Illustrated biochemistry, 30th Edition]



It is a ligation reaction.

39. d) Biotin

Vitamin H= Biotin

Functions :

Coenzyme in carboxylation reactions in gluconeogenesis and fatty acid synthesis; role in regulation of cell cycle

Deficiency disease:

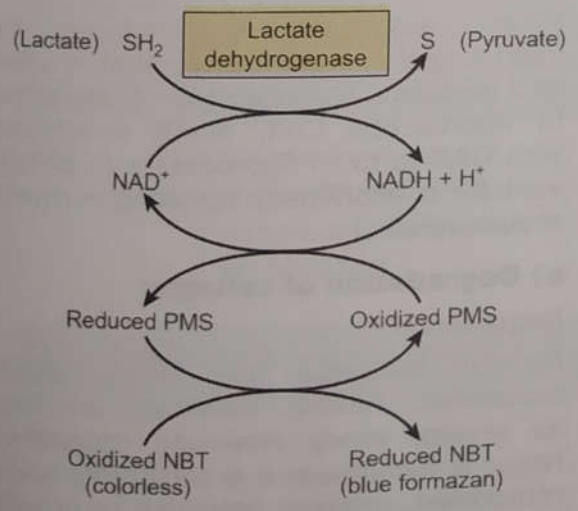
Impaired fat and carbohydrate metabolism, dermatitis

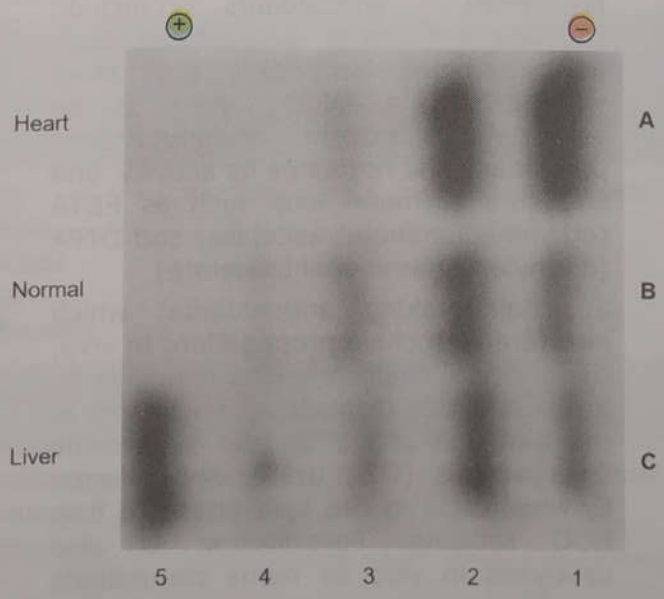
40. d) LDH-5

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Lactate dehydrogenase (LDH) is a tetrameric enzyme consisting of two monomer types: H (for heart) and M (for muscle) that combine to yield five LDH isozymes: HHHH (I1), HHHM (I2), HHMM (I3), HMMM (I4), and MMMM (I5). Tissue-specific expression of the H and M genes determines the relative proportions of each subunit in different tissues. Isozyme I1 predominates in heart tissue, and isozyme I5 in liver. Thus, tissue injury releases a characteristic pattern of LDH isozymes that can be separated by electrophoresis and detected using a coupled assay.

Today, LDH has been superseded as a marker for MI by other proteins that appear more rapidly in plasma.





Normal and pathologic patterns of lactate dehydrogenase (LDH) isozymes in human serum. LDH isozymes of serum were separated by electrophoresis and visualized using the coupled reaction scheme shown on the left. (NBT, nitroblue tetrazolium; PMS, phenazine methylsulfate.)

At right is shown the stained electropherogram. Pattern A is serum from a patient with a myocardial infarct; B is normal serum; and C is serum from a patient with liver disease. Arabic numerals denote specific LDH isozymes.

41. c) Molybdenum

Examples of flavoprotein enzymes include L-amino acid oxidase, an FMN-linked enzyme found in kidney with general specificity for the oxidative deamination of the naturally occurring L-amino acids; xanthine oxidase, which contains molybdenum and plays an important role in the conversion of purine bases to uric acid and is of particular significance in uricotelic animals and aldehyde dehydrogenase, an FAD-linked enzyme present in mammalian livers, which contains molybdenum and nonheme iron and acts upon aldehydes and N-heterocyclic substrates.

42. b) Antioxidant

Antioxidants fall into two classes:

1. preventive antioxidants, which reduce the rate of chain initiation

Preventive antioxidants include catalase and other peroxidases such as glutathione peroxidase that react with ROOH; selenium, which is an essential component of glutathione peroxidase and regulates its activity, and chelators of metal ions such as EDTA (ethylenediaminetetraacetate) and DTPA (diethylenetriaminepentaacetate).

2. chainbreaking antioxidants, which interfere with chain propagation. In vivo, the principal chain-breaking antioxidants are superoxide dismutase, which acts in the aqueous phase to trap superoxide free radicals ($O_2^{\cdot}$) urate, and vitamin E, which acts in the lipid phase to trap ROO radicals. Peroxidation is also catalyzed in vivo by heme compounds and by lipoxygenases found in platelets and leukocytes. Other products of auto-oxidation or enzymic oxidation of physiologic significance include oxysterols (formed from cholesterol) and isoprostanes (formed from the peroxidation of polyunsaturated fatty acids such as arachidonic acid).

43. c) Protein moiety

Some enzymes require molecules other than proteins for enzymic activity.

The term holoenzyme refers to the active enzyme with its nonprotein component, whereas the enzyme without its nonprotein moiety is termed an apoenzyme and is inactive.

If the nonprotein moiety is a metal ion, such as Zn^{2+} or Fe^{2+}, it is called a cofactor. If it is a small organic molecule, it is termed a coenzyme.

Coenzymes that only transiently associate with the enzyme are called co-substrates. Co-substrates dissociate from the enzyme in an altered state .

If the coenzyme is per manently associated with the enzyme and returned to its original form, it is called a prosthetic group .

Coenzymes commonly are derived from vitamins. For example, NAD+ contains niacin, and FAD contains riboflavin .

44. b) Competitive

Isomerization of citrate

Citrate is isomerized to isocitrate by aconitase (aconitate hydratase), an Fe-S protein.

[Note: Aconitase is inhibited by fluoroacetate, a plant toxin that is used as a pesticide. Fluoroacetate is converted to fluoroacetyl CoA, which condenses with OAA to form fluorocitrate (a potent inhibitor of aconitase), resulting in citrate accumulation.]

45. a) Degradation of collagen

Degradation

Normal collagens are highly stable molecules, having half-lives as long as several years. However, connective tissue is dynamic and is constantly being remodeled, often in response to growth or injury of the tissue. Breakdown of

collagen fibers is dependent on the proteolytic action of collagenases, which are part of a large family of matrix metalloproteinases. For type I collagen, the cleavage site is specific, generating three-quarter and one-quarter length fragments. These fragments are further degraded by other matrix proteinases.

46. a) 1

[Ref: Lippincott's illustrated reviews, 6th Edition]

Osteogenesis imperfecta: This syndrome, known as brittle bone disease, is a genetic disorder of bone fragility characterized by bones that fracture easily, with minor or no trauma .Over 80% of cases of osteogenesis imperfecta (OI) are caused by dominant mutations to the genes that code for the α1 or α2 chains in type I collagen.

47. b) Cystine

These are present in exoskeletal structures e.g. hair, nails, horns. Human hair keratin contains as much as 14% cysteine.

48. c) Zinc

[Ref: Satyanarayan 4th Edition]

Metalloenzymes :

These enzymes hold the metals rather tightly which are not readily exchanged.

e.g. alcohol dehydrogenase, carbonic anhydrase, alkaline phosphatase, carboxypeptidase and aldolase contain zinc.

Phenol oxidase (copper);
Pyruvate oxidase (manganese);
Xanthine oxidase (molybdenum);
Cytochrome oxidase (iron and copper).

Element	Major functions	Deficiency/ disease symptoms	Recommendeddisease dietary allowance	Major sources
Iron	Constituent of hemee.g. hemoglobin, myoglobin,cytochromes; involved in 0_2transport and biologicaloxidation.	Hypochromic, microcyticanemia	10-15 mg/d	Organ meats (liver, heart),leafy vegetables, iron cookware
Copper	Constituent of enzymese.g. cytochrome C oxidase,catalase, tyrosinase; in irontransport.	Anemia, Menke's disease	2-3 mg/d	Organ meats cereals, leafyvegetables
Iodine	Constituent of thyroxine andtriiodothyronine	Cretinism, goiter, myxedema	150-200 µg/d	Iodized salt, sea foods
Manganese	Cofactor for enzymese.g. arginase. pyruvatecarboxylase; glycoproteinsynthesis.	Almost unknown	2-9 mg/d	Cereals, leafy vegetables
Zinc	Cofactor for enzymese.g. alcohol dehydrogenase, carbonic anhydrase, lactate dehydrogenase.	Growth retardation, poorwound healing, hypogonadism	10-15 mg/d	Meat, fish, milk
Molybdenum	Constituent of enzymese.g. xanthine oxidase	Almost unknown	75-250 µg/d	Vegetables
Cobalt	Constituent of vitamin B_{12},required for the formationof erythrocytes	Pernicious anemia (as invitamin B_{12} deficiency)	5-8 µg/d	Foods of animal origin

Fluorine	Helps in the proper formationof bones and teeth	Dental caries, osteoporosis	2-4 mg/d	Drinking water
Selenium	Involved in antioxidantfunction along with vitamin E;constituent of glutathioneperoxidase and selenocysteine	Muscular degeneration, cardiomyopathy	50-200 µg/d	Organ meats, sea foods
Chromium	Promotes insulin function(as glucose tolerance factor)	Impaired glucose tolerance	10-100 µg/d	Brewer's yeast, meat, wholegrains

49. d) Endoplasmic retinaculum

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Collagen Undergoes Extensive Posttranslational Modifications :

- Newly synthesized collagen undergoes extensive posttranslational modification before becoming part of a mature extracellular collagen fiber
- Like most secreted proteins, collagen is synthesized on ribosomes in a precursor form, preprocollagen, which contains a leader or signal sequence that directs the polypeptide chain into the lumen of the endoplasmic reticulum.
- As it enters the endoplasmic reticulum, this leader sequence is enzymatically removed.
- Following secretion from the cell by way of the Golgi apparatus, extracellular enzymes called procollagen aminoproteinase and procollagen carboxyproteinase remove the extension peptides at the amino and carboxyl terminal ends, respectively.
- Cleavage of these propeptides may occur within crypts or folds in the cell membrane. Once the propeptides are removed, the triple helical collagen molecules, containing approximately 1000 amino acids per chain, spontaneously assemble into collagen fibers.
- These are further stabilized by the formation of inter- and intrachain cross-links through the action of lysyl oxidase, as described previously. The same cells that secrete collagen also secrete fibronectin, a large glycoprotein present on cell surfaces, in the extracellular matrix, and in blood (see below).

Intracellular
1. Cleavage of signal peptide.
2. Hydroxylation of prolyl residues and some lysyl residues; glycosylation of some hydroxylysyl residues.
3. Formation of intrachain and interchain S-S bonds in extension peptides.
4. Formation of triple helix.
Extracellular
1. Cleavage of amino and carboxyl terminal propeptides.
2. Assembly of collagen fibers in quarter-staggered alignment.
3. Oxidative deamination of £-amino groups of lysyl and hydroxylysyl residues to aldehydes.
4. Formation of intra- and interchain cross-links via Schiff bases and aldol condensation products.

50. d) Aminopeptidase

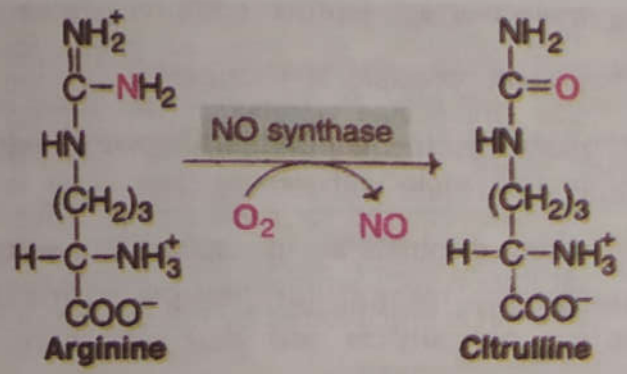
- Endopeptidases hydrolyze peptide bonds between specific amino acids throughout the molecule. They are the first enzymes to act, yielding a larger number of smaller fragments. Pepsin in the gastric juice catalyzes hydrolysis of peptide bonds adjacent to aromatic and branched-chain amino acids and methionine. Trypsin, chymotrypsin, and elastase are secreted into the small intestine by the pancreas. Trypsin catalyzes hydrolysis of lysine and arginine esters, chymotrypsin esters of aromatic amino acids, and elastase esters of small neutral aliphatic amino acids.

51. d) Requires NADH, FAD, FMN & Heme iron

[Ref: Satyanarayan 4th Edition]

The reaction catalyzed by nitric oxide synthase, a five-electron oxidoreductase with multiple cofactors, converts one nitrogen of the guanidine group of arginine to nitric oxide (NO), an intercellular signaling molecule that serves as a neurotransmitter, smooth muscle relaxant, and vasodilator .

L-Arginine + NADPH + H+ + O2 → NO + Citrulline + NADP+



52. a) Glutamate dehydrogenase

- The peroxisome is bounded by a single membrane and contains more than 50 enzymes; catalase and urate oxidase are marker enzymes for this organelle.
- Hexokinase is the marker enzyme for cytosol.
- DNA polymerase is the marker enzyme for nucleus.
- glutamate dehydrogenase and glucose 6-phosphatase are the markers for mitochondria and ribosomes, respectively.
- Cardiac troponins thus serves as a marker of all heart muscle damage. The search for additional markers for heart disease, such as ischemia modified albumin.

Membrane	Enzyme
Plasma	5'-Nucleotidase Adenylyl cyclase Na+-K+-ATPase
Endoplasmic reticulum	Glucose-6-phosphatase
Golgi apparatus Cis Medial Trans TGN	GlcNAc transferase 1 Golgi mannosidase II Galactosyl transferase Sialyl transferase
Inner mitochondrial membrane	ATP synthase

53. d) Glucose

Glucose oxidase test : This is a strip test for the specific detection of glucose. The enzyme glucose oxidase oxidizes glucose to liberate hydrogen peroxide which in turn is converted to nascent oxygen (O-) by peroxidase enzyme. The compound O-diansidine combines with nascent oxygen to form a coloured (yellow to red) complex.

54. c) Enterokinase

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Function	Plasma Proteins
Antiproteases	Antichymotrypsin α-Antitrypsin (α_1-antiproteinase) α_2-Macroglobulin Antithrombin

55. c) Hydroxyproline
d) Glycine

[Ref: Harper's Illustrated biochemistry, 30th Edition]

Collagen is also rich in proline and hydroxyproline, yielding a repetitive Gly-X-Y pattern in which Y generally is proline or hydroxyproline.

Amino acid sequence –Gly – X – Y – Gly – X – Y – Gly – X – Y –

2° structure

Triple helix

Collagen triple helices are stabilized by hydrogen bonds between residues in different polypeptide chains, a process aided by the hydroxyl groups of hydroxyprolyl residues. Additional stability is provided by covalent cross-links formed between modified lysyl residues both within and between polypeptide chains.

56. d) Hemoglobin

Collagen is the most abundant protein in the animal world

Collagen, the major component of most connective tissues, constitutes

approximately 25% of the protein of mammals. It provides an extracellular framework for all metazoan animals and exists in virtually every animal tissue. At least 28 distinct types of collagen made up of over 30 distinct polypeptide chains (each encoded by a separate gene) have been identified in human tissues.

57. c) Inter relation and arrangement of polypeptides in a protein with more than 2 polypetide chain

Quaternary structure defines the polypeptide composition of a protein and, for an oligomeric protein, the spatial relationships between its protomers or subunits. Monomeric proteins consist of a single polypeptide chain. Dimeric proteins contain two polypeptide chains. Homodimers contain two copies of the same polypeptide chain, while in a heterodimer the polypeptides differ. Greek letters (α, β, γ, etc.) are used to distinguish different subunits of a heterooligomeric protein, and subscripts indicate the number of each subunit type. For example, α4 designates a homotetrameric protein, and α2β2γ a protein with five subunits of three different types.

58. b) Have specific genetic code

The proteins on degradation (proteolysis) release individual amino acids. Amino acids are not just the structural components of proteins. Each one of the 20 naturally occurring amino acids which are coded by 61 codons undergoes its own metabolism and performs specific functions. Some of the amino acids also serve as precursors for the synthesis of many biologically important compounds (e.g melanin, serotonin, creatine etc.). Certain amino acids may directly act as neurotransmitters (e.g. glycine aspartate, glutamate).

59. c) Leucine

Those amino acids that give rise to acetyl-CoA are referred to as ketogenic, because in prolonged fasting and starvation much of the acetylCoA is used for synthesis of ketone bodies in the liver.

Leucine –is purely Ketogenic.

60. a) Salting out

Precipitation by neutral salts :

The process of protein precipitation by the addition of neutral salts such as ammonium sulfate or sodium sulfate is referred to as salting out. This phenomenon is explained on the basis of dehydration of protein molecules by salts. This causes increased protein -protein interaction, resulting in molecular aggregation and precipitation. The amount of salt required for protein precipitation depends on the size (molecular weighg of the protein molecule. In general, the higher is the protein molecular weight, the lower is the salt required for precipitation. Thus, serum globulins are precipitated by half saturation with ammonium sulfate while albumin is precipitated by full saturation.

61. c) Bicarbonate

Anion gap-

- (7–16 mmol/L)
- The anion gap is calculated from plasma $Na+ - [Cl^- + HCO3^-]$

62. d) Retinol binding protein

63. c) SDS-PAGE

a. Electrophoresis-

Electrophoresis separates charged biomolecules based on the rates at which they migrate in an applied electrical field.

b. Salting out-

The process of protein precipitation by the addition of neutral salts such as ammonium sulfate or sodium sulfate is referred to as salting out. This phenomenon is explained on the basis of dehydration of protein molecules by salts. This causes increased protein -protein interaction, resulting in molecular aggregation and precipitation.

c. SDS-PAGE –

The most widely used method for determining the purity of a protein is SDS-PAGE—polyacrylamide gel electrophoresis (PAGE) in the presence of the anionic detergent sodium dodecyl sulfate (SDS). Electrophoresis separates charged biomolecules based on the rates at

which they migrate in an applied electrical field. SDS denatures and binds to proteins at a ratio of one molecule of SDS per two peptide bonds. The large number of anionic SDS molecules, each bearing a charge of −1, overwhelms the charge contributions of the amino acid functional groups endogenous to the polypeptides. Since the charge-to-mass ratio of each SDS-polypeptide complex is approximately equal, the physical resistance each peptide encounters as it moves through the acrylamide matrix determines the rate of migration. Since large complexes encounter greater resistance, polypeptides separate based on their relative molecular mass (Mr). Individual polypeptides trapped in the acrylamide gel are visualized by staining with dyes such as Coomassie blue.

d. Ion exchange chromatography-

Ion Exchange Chromatography In ion exchange chromatography, proteins interact with the stationary phase by charge-charge interactions. Proteins with a net positive charge at a given pH adhere to beads with negatively charged functional groups such as carboxylates or sulfates (cation exchangers). Similarly, proteins with a net negative charge adhere to beads with positively charged functional groups, typically tertiary or quaternary amines (anion exchangers).

64. c) Golgi apparatus

The Golgi Apparatus Is Involved in Glycosylation & Sorting of Proteins The GA plays two major roles in membrane synthesis. First, it is involved in the processing of the oligosaccharide chains of membrane and other N-linked glycoproteins and also contains enzymes involved in O-glycosylation .

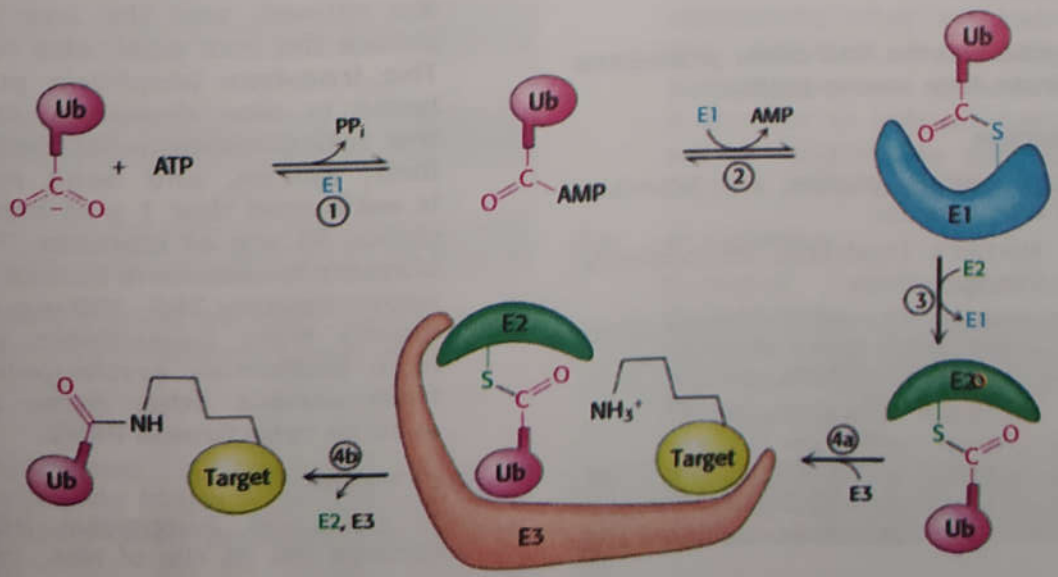
Second, it is involved in the sorting of various proteins prior to their delivery to their appropriate intracellular destinations. All parts of the GA participate in the first role, whereas the trans Golgi network (TGN) is particularly involved in the second and is very rich in vesicles.

65. b) Proteasomes

[Ref: Stryer 8th Edition]

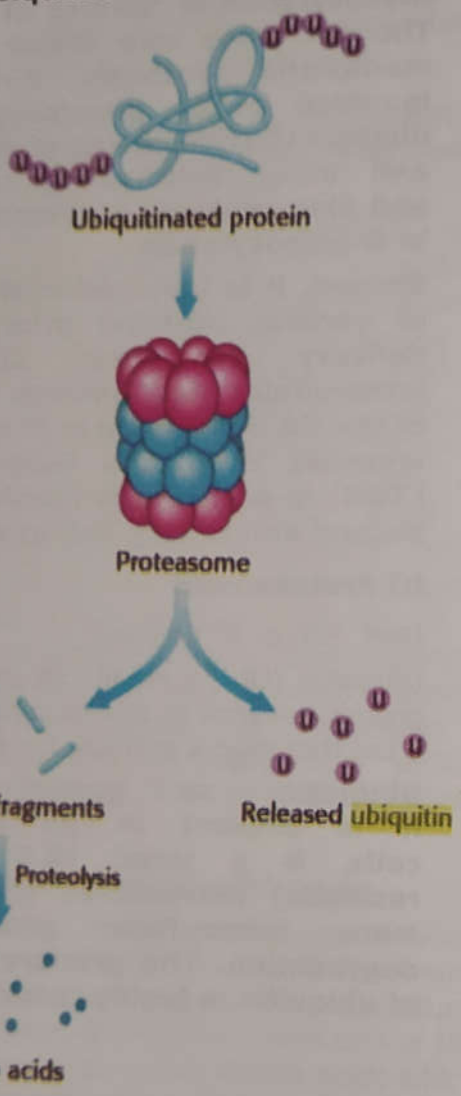
Ubiquitin (Ub), a small (76 amino acids) protein present in all eukaryotic cells, is a tag that marks proteins for destruction.

Ubiquitin, so named because it is present in all eukaryotic cells, is a small (8.5 kDa, 76 residues) polypeptide that targets many intracellular proteins for degradation. The primary structure of ubiquitin is highly conserved.



Ubiquitin conjugation.

Subsequent degradation of ubiquitin-tagged proteins takes place in the proteasome, a macromolecule with multiple different subunits that also is ubiquitous in eukaryotic cells.

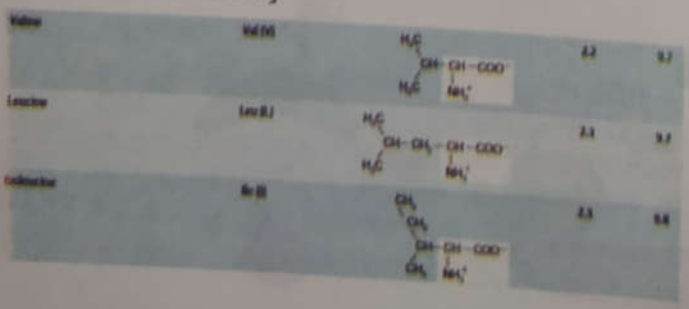


The proteasome and other proteases generate free amino acids.

66. c) Leucine

Because valine ,leucine are branched chain amino acids.

[Ref: Harper's Illustrated Biochemistry, 29th edition]



67. b) Histidine

[Ref: Harper's Illustrated Biochemistry, 29th edition]

Histidine plays unique roles in enzymatic catalysis. The pKa of its imidazole proton permits it to function at neutral pH as either a base or an acid catalyst.

Typical Range of pKa Values for Ionizable Groups in Proteins.

Dissociating Group	pK_a Range
α-Carboxyl	3.5-4,0
Non-α COOH of AsporGlu	4.0-4.8
Imidazole of His	6.5-7,4
SH of Cys	8.5-9.0
OH of Tyr	9.5-10.5
α-Amino	8.0-9.0
ε-Amino of Lys	9.8-10.4
Guanidinium of Arg	~12.0

68. a) 8 gm

Under physiologic conditions in the human adult, 1–2 × 108 erythrocytes are destroyed per hour. Thus, in 1 day, a 70-kg human turns over approximately 6 g of hemoglobin. When hemoglobin is destroyed in the body, globin is degraded to its constituent amino acids, which are reused, and the iron of heme enters the iron pool, also for reuse. The iron-free porphyrin portion of heme is also degraded, mainly in the reticuloendothelial cells of the liver, spleen, and bone marrow.It is estimated that 1 g of hemoglobin yields 35 mg of bilirubin. The daily bilirubin formation in human adults is approximately 250–350 mg, deriving mainly from hemoglobin but also from ineffective erythropoiesis and from various other heme proteins such as cytochrome P450.

69. c) Valine

In sickle cell hemoglobin (HbS), Val replaces the β6 Glu of HbA, creating a

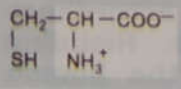
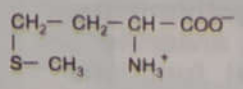
"sticky patch" that has a complement on deoxyHb (but not on oxyHb). DeoxyHbS polymerizes at low O2 concentrations, forming fibers that distort erythrocytes into sickle shapes.

70. a) Glycine
c) Glutamate

Glutathione (γ- glutamyl- cysteinyl-glycine). Note the non-α peptide bond that links Glu to Cys.

71. a) Cystein
d) Methionine

[Ref: Harper's Illustrated Biochemistry, 29th edition]

With Side Chains Containing Sulfur Atoms					
Cysteine	Cys [C]		1.9	10.8	8.3
Methionine	Met [M]		2.1	9.3	

72. d) Arginine
e) Histidine

[Ref: Harper's Illustrated Biochemistry, 29th edition]

Nutritionally Essential	Nutritionally Nonessential
Arginine[1]	Alanine
Histidine	Asparagine
Isoleuciine	Aspartate
Leucine	Cysteine
Lysine	Glutamate
Methionine	Glutamine
Phenylalanine	Glycine
Threonine	Hydroxyproline[2]
Tryptophan	Hydroxy lysine[2]
Valine	Proline
	Serine
	Tyrosine

73. a) Mediators of the post-translational assembly of protein complexes

[Ref: Harper's Illustrated Biochemistry, 29th edition]

Chaperones Chaperone proteins participate in the folding of over half of mammalian proteins. The hsp70 (70-kDa heat shock protein) family of chaperones binds short sequences of hydrophobic amino acids in newly synthesized polypeptides, shielding them from solvent. The hsp60 family of chaperones, sometimes called chaperonins, differ in sequence and structure from hsp70 and its homologs. Hsp60 acts later in the folding process, often together with an hsp70 chaperone. The central cavity of the donut-shaped hsp60 chaperone provides a sheltered environment in which a polypeptide can fold until all hydrophobic regions are buried in its interior, eliminating aggregation.

Translocation occurs posttranslationally, after the matrix proteins are released from the cytosolic polyribosomes. Interactions with a number of cytosolic proteins that act as chaperones and as targeting factors occur prior to translocation.

74. d) Cysteine

Cysteine participates in the biosynthesis of coenzyme A by reacting with pantothenate to form 4-phosphopantothenoyl-cystein. Three enzyme-catalyzed reactions convert cysteine to taurine, which can displace the coenzyme A moiety of cholyl-CoA to form the bile acid taurocholic acid.

75. b) Muscle

Histidine

Decarboxylation of histidine by the pyridoxal 5′-phosphatedependent enzyme histidine decarboxylase forms histamine. A biogenic amine that functions in allergic reactions and gastric secretion, histamine is present in all tissues. Its concentration in the brain hypothalamus varies in accordance with a circadian rhythm. Histidine compounds present in the human body include ergothioneine, carnosine, and dietary anserine . While their physiological functions are unknown, carnosine (β-alanyl-histidine) and homocarnosine (γ-aminobutyryl-histidine) are major constituents of excitable tissues, brain, and skeletal muscle. Urinary levels of 3-methylhistidine are unusually low in patients with Wilson's disease.

76. d) Selenocysteine

Selenocysteine, the 21st Amino Acid While its occurrence in proteins is uncommon, selenocysteine is present at the active site of several human enzymes that catalyze redox reactions. Examples include thioredoxin reductase, glutathione peroxidase, and the deiodinase that converts thyroxine to triiodothyronine.

77. c) Alanine

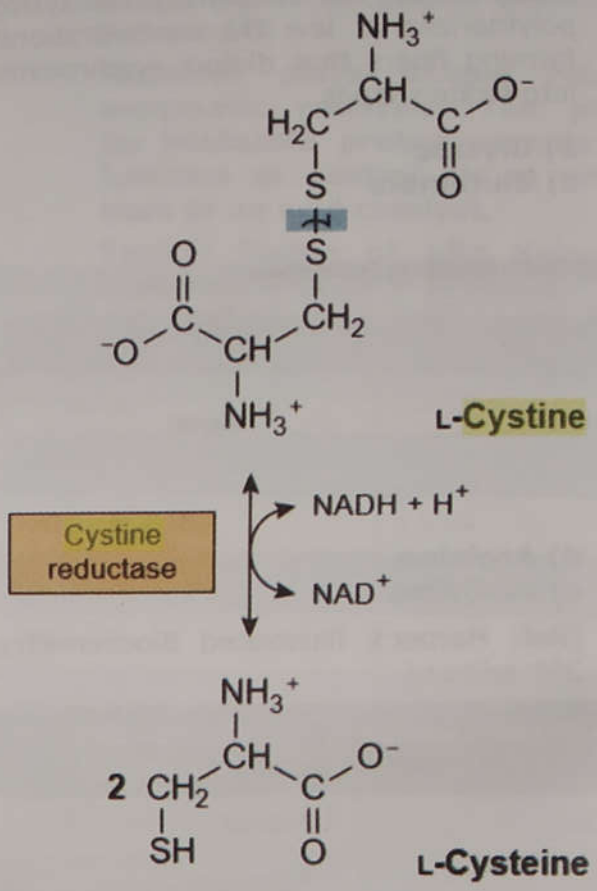
[Ref: Harper's Illustrated Biochemistry, 29th edition]

Biosynthesis of creatine and creatinine. Conversion of glycine and the guanidine group of arginine to creatine and creatine phosphate. Also shown is the nonenzymic hydrolysis of creatine phosphate to creatine.

78. d) Disulfide bond between cysteine molecule

[Ref: Harper's Illustrated Biochemistry, 29th edition]

The cystine reductase reaction:

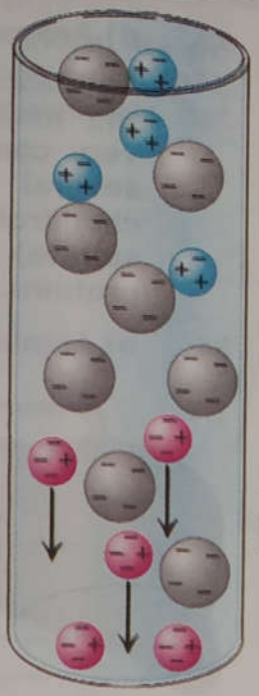


79. b) Charge

[Ref: Stryer 8th Edition]

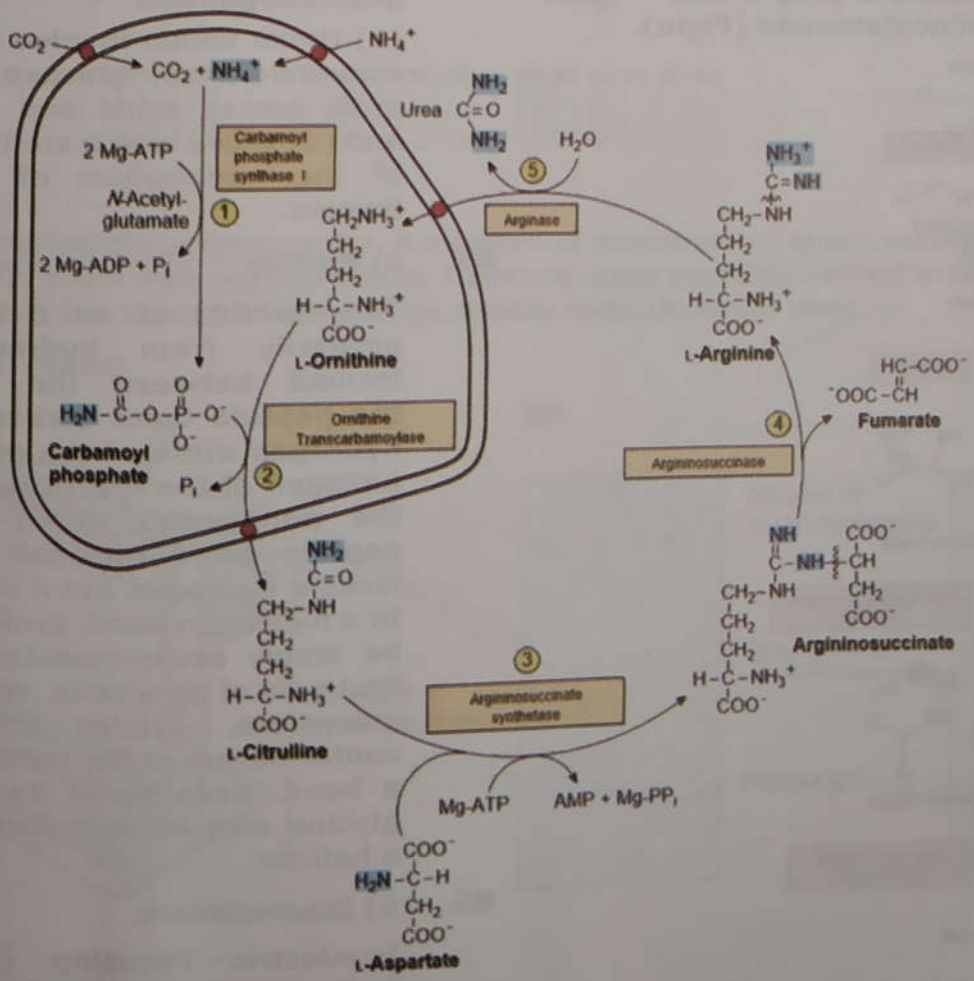
Ion Exchange Chromatography:

In ion exchange chromatography, proteins interact with the stationary phase by charge-charge interactions. Proteins with a net positive charge at a given pH adhere to beads with negatively charged functional groups such as carboxylates or sulfates (cation exchangers). Similarly, proteins with a net negative charge adhere to beads with positively charged functional groups, typically tertiary or quaternary amines (anion exchangers). Proteins, which are polyanions, compete against monovalent ions for binding to the support—thus the term "ion exchange." For example, proteins bind to diethylaminoethyl (DEAE) cellulose by replacing the counter-ions (generally Cl– or CH3COO–) that neutralize the protonated amine.



Ion-exchange chromatography. This technique separates proteins mainly according to their net charge.

80. d) NH3 and aspartate



2 Sources of Nitrogen of urea Cycle:

1.NH^{4+}

2.Aspartate

81. a) Light chains

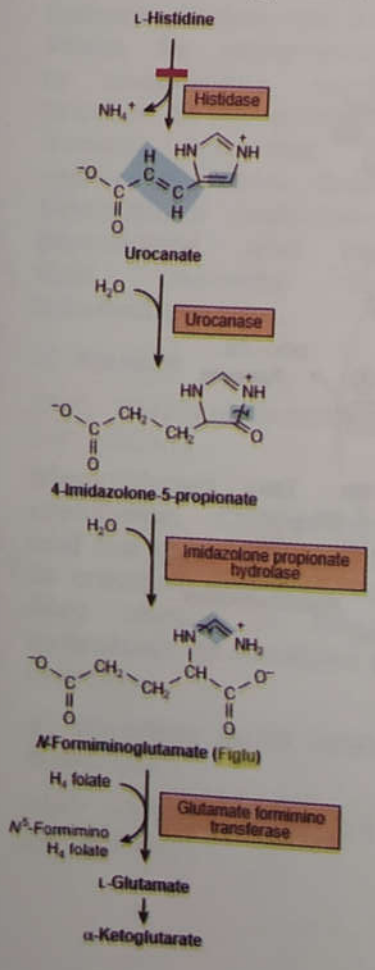
Bence fones proteins : Henry Bence Jones first described them in 1847. These are the light chains (KAPPA or LAMDA) of immunoglobulins that are synthesized in excess. Bence Jones proteins have a molecular weight of 20,000 or 40,000 (for dimer). In about 20% of the patients of multiple myeloma, Bence Jones proteins are excreted in urine which often damages the renal tubules.

82. a) Histidine

[Ref: Harper's Illustrated Biochemistry, 29th edition]

Histidine

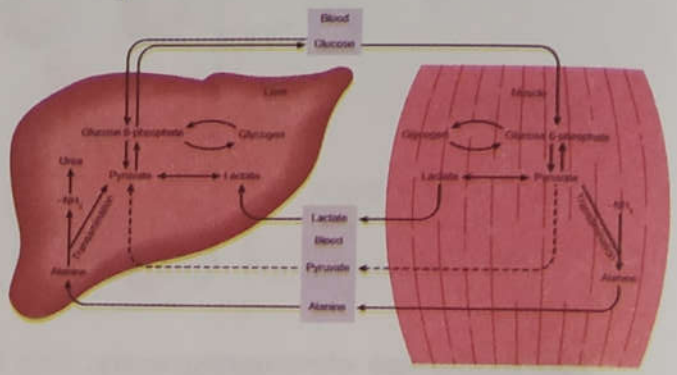
Catabolism of histidine proceeds via urocanate, 4-imidazolone-5-propionate, and N-formiminoglutamate (Figlu).



83. d) Proteoglycan found in cartilage

Aggrecan (about 2 × 103 kDa) is the major proteoglycan. It has a very complex structure, containing several GAGs (hyaluronic acid, chondroitin sulfate, and keratan sulfate) and both link and core proteins.

84. a) Alanine



Glucose is formed from two groups of compounds that undergo gluconeogenesis

(1) those which involve a direct net conversion to glucose, including most amino acids and propionate; and (2) those which are the products of the metabolism of glucose in tissues.

85. c) Proline

The stability of an α helix arises primarily from hydrogen bonds formed between the oxygen of the peptide bond carbonyl and the hydrogen atom of the peptide bond nitrogen of the fourth residue down the polypeptide chain. Since the peptide bond nitrogen of proline lacks a hydrogen atom to contribute to a hydrogen bond, proline can only be stably accommodated withinthe first turn of an α helix. When present elsewhere, proline disrupts the conformation of the helix, producing a bend. Because of its small size, glycine also often induces bends in α helices.

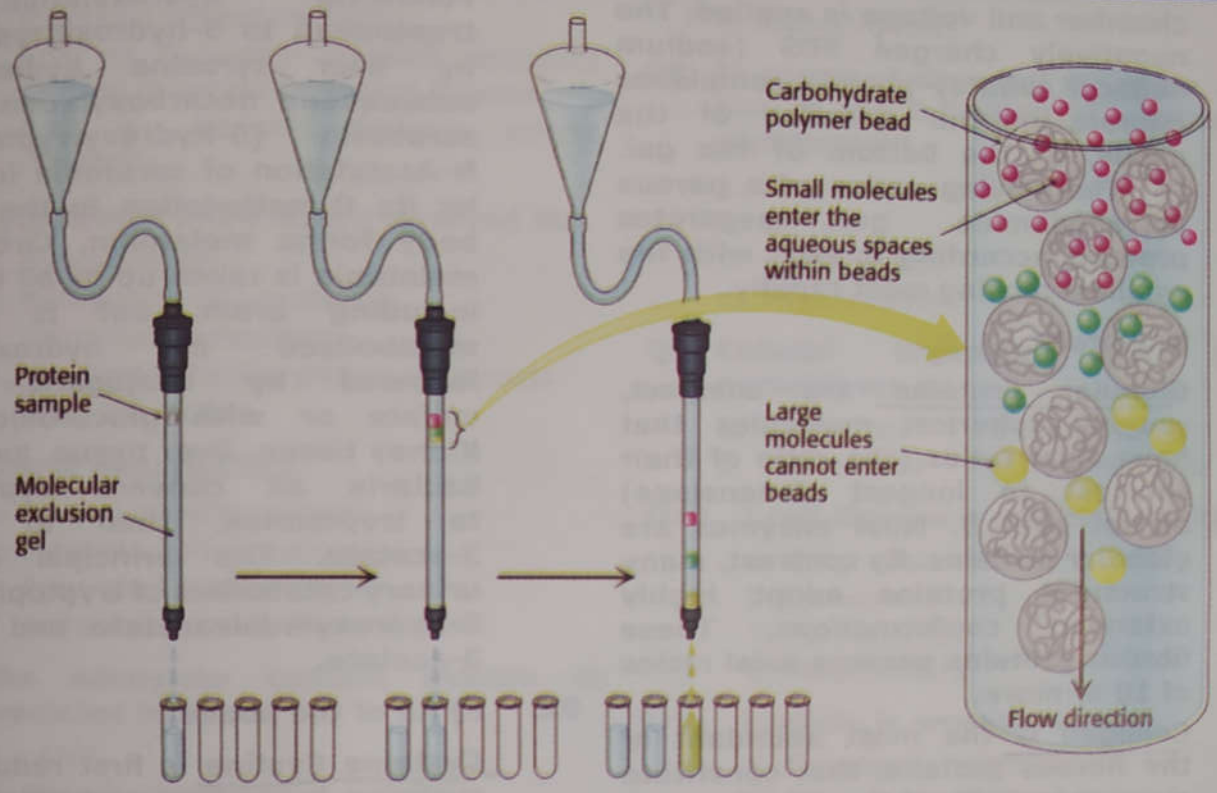
86. b) Isoelectectric

Isoelectric Focusing (IEF) Ionic buffers called ampholytes and an applied electric field are used to

generate a pH gradient within a polyacrylamide matrix. Applied proteins migrate until they reach the region of the matrix where the pH matches their isoelectric point (pI), the pH at which a molecule's net charge is zero

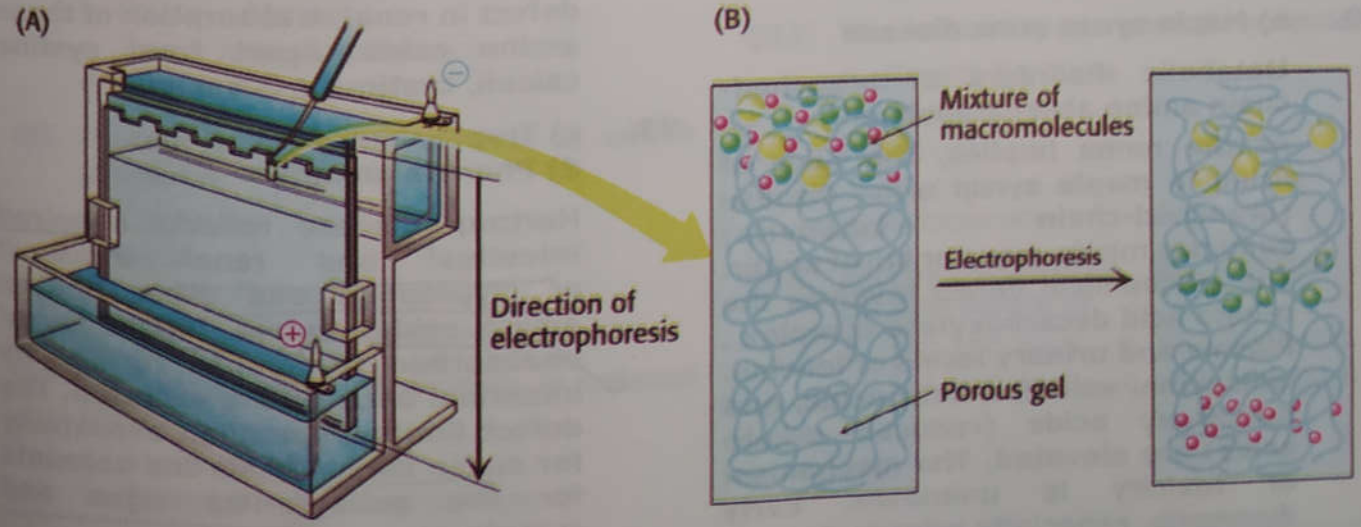
87. c) Gel diffusion chromatography

Gel-filtration chromatography. More-discriminating separations on the basis of size can be achieved by the technique of gel-filtration chromatography, also known as molecular exclusion chromatography.



Gel-filtration chromatography. A mixture of proteins in a small volume is applied to a column filled with porous beads. Because large proteins cannot enter the internal volume of the beads, they emerge sooner than do small ones.

88. a) SDS – PAGE



Polyacrylamide gel electrophoresis.

(A) Gelelectrophoresis apparatus. Typically, several samples undergo electrophoresis on one flat polyacrylamide gel. A microliter pipette is used to place solutions of proteins in the wells of the slab. A cover is then placed over the gel chamber and voltage is applied. The negatively charged SDS (sodium dodecyl sulfate)–protein complexes migrate in the direction of the anode, at the bottom of the gel. (B) The sieving action of a porous polyacrylamide gel separates proteins according to size, with the smallest moving most rapidly.

89. b) Fibrous

Globular proteins are compact, roughly spherical molecules that have axial ratios (the ratio of their shortest to longest dimensions) of not over 3. Most enzymes are globular proteins. By contrast, many structural proteins adopt highly extended conformations. These fibrous proteins possess axial ratios of 10 or more.

Collagen is the most abundant of the fibrous proteins that constitute more than 25% of the protein mass in the human body. Other prominent fibrous proteins include keratin and myosin. These fibrous proteins represent a primary source of structural strength for cells (ie, the cytoskeleton) and tissues.

90. a) Maple syrup urine disease

Metabolic disorders of branched-chain amino acid catabolism

As the name implies, the odor of urine in maple syrup urine disease (branched-chain ketonuria) suggests maple syrup or burnt sugar. The biochemical defect involves the α-keto acid decarboxylase complex . Plasma and urinary levels of leucine, isoleucine, valine, α-keto acids, and α-hydroxy acids (reduced α-keto acids) are elevated. The mechanism of toxicity is unknown. Early diagnosis, especially prior to 1 week of age, employs enzymatic analysis. Prompt replacement of dietary protein by an amino acid mixture that lacks leucine, isoleucine, and valine averts brain damage and early mortality.

91. a) Tryphophan

Following hydroxylation of tryptophan to 5-hydroxytryptophan by liver tyrosine hydroxylase, subsequent decarboxylation forms serotonin (5-hydroxytryptamine), N-Acetylation of serotonin followed by its O-methylation in the pineal body forms melatonin. Circulating melatonin is taken up by all tissues, including brain, but is rapidly metabolized by hydroxylation followed by conjugation with sulfate or with glucuronic acid. Kidney tissue, liver tissue, and fecal bacteria all convert tryptophan to tryptamine, then to indole 3-acetate. The principal normal urinary catabolites of tryptophan are 5-hydroxyindoleacetate and indole 3-acetate.

92. e) All of the above

Cysteine Cystine is first reduced to cysteine by cystine reductase. Two different pathways then convert cysteine to pyruvate. There are numerous abnormalities of cysteine metabolism. Cystine, lysine, arginine, and ornithine are excreted in cystine-lysinuria (cystinuria), a defect in renal re absorption of these amino acids. Apart from cystine calculi, cystinuria is benign.

93. c) Tryptophan
d) Phenylalamnine

Hartnup disease reflects impaired intestinal and renal transport of tryptophan and other neutral amino acids. Indole derivatives of unabsorbed tryptophan formed by intestinal bacteria are excreted. The defect limits tryptophan availability for niacin biosynthesis and accounts for the pellagra-like signs and symptoms.

Miscellaneous – Questions

Q1. True statement about insulin:

a. It acts on nuclear membrane receptor
b. It acts on steroid receptor
c. Acts on G-protein coupled receptors coupled to serine threonine kinases
d. Acts on intrinsic tyrosine kinase receptors

Q2. Cytochrome P450 is/are involved in:

a. Hydroxylation
b. Methylation of xenobiotics
c. Deamination reaction
d. Involved in hydroxylation of steroids
e. Drug interaction

Q3. Zinc is required for:

a. Alcohol dehydrogenase
b. Pyruvate dehydrogenase
c. Pyruvate Decarboxylase
d. Alpha keto acid Dehydrogenase

Q4. The adenylate cyclase system is mediated by:

a. cAMP
b. Phosphodiesterase
c. GTP regulating proteins
d. Nuclear receptors

Q5. Which of the following deficiencies does not match the clinical situation?

a. Iron – Anemia
b. Folate – Anemia
c. Zinc – Immunodeficiency
d. Selenium – Dry skin

Q6. Protein acts as buffer due to which property-

a. Colloid
b. Basic
c. Acidic
d. Amphipathic (amphoteric in nature)

Q7. Biological value of protein is related to:

a. Amino acid content
b. Essenital amino acid content
c. N2 content
d. Content of NH3 to uria
e. Protein quality

Q8. In terms of chemical structure which one of the following is a tetrameric glycoprotein –

a. Insulin receptors
b. Leptins
c. Neuropeptide
d. Thyrotrophin

Q9. Cellular organelle that stores peroxidases is

a. Lysozomes b. Peroxisome
c. Microsomes d. Mitochandria

Q10. I cell disease is associated with

a. Golgi apparatus
b. Lysosomes
c. Peroxisomes
d. Mitochondria

Q11. Laminin is present in

a. Basement membrane
b. Inner nuclear membrane
c. Outer nuclear membrane
d. Mitochondria

Q12. All are glycoprotein, except

a. TSH b. FSH
c. LH d. GH

Q13. The following are protein hormones

a. Growth hormone
b. Corticosteroids
c. Insulin
d. Glucagon
e. Aldosterone

Q14. Microalbuminuria is defined as protein levels of

a. 100-150 mg/L b. 151-200 mg/L
c. 201-300 mg/L d. 301-600 mg/L

1. d	2. a, c, d, e	3. a	4. c	5. d	6. d	7. e	8. a	9. b
10. b	11. a	12. d	13. a,c,d	14. b				

Q15. Following statement about biological membrane is correct

a. They are symmetric bileaflet structure
b. They constituent lipid & Protein moieties are held together by covalent interaction
c. They are rigid assemblies of protein; lipid & carbohydrates
d. Their lipid moieties are amphipathic in nature

Q16. Bilayer cell membrane contains

a. Cholesterol
b. Triacyl glycerol
c. Cholesterol ester
d. Glycerol

Q17. The most important buffer in extracellular fluid is:

a. Hemoglobin
b. Protein
c. Phosphate
d. Bicarbonate buffer

Q18. True about oxygenase enzyme are all except?

a. Incorporates one oxygen atom in the substrate
b. Incorporates two oxygen in the substrate
c. Involved in hydroxylation reaction
d. Involved in carboxylation of drugs

Q19. In Reye's syndrome, typical histopathological appearance is due to defects in

a. Beta oxidation of fatty acids
b. Urea cycle
c. Mitchondria
d. ETC chain

Q20. The conversion of optically pure isomer (enantiomer) into a mixture of equal amounts of both dextro and levo forms is called as –

a. Polymerization
b. Stereoisomerization
c. Racemization
d. Fractionation

Q21. Mature erythrocyte possesses

a. Lecithin
b. Ganglioside
c. Hemoglobin
d. ATP
e. All of the above

Q22. Black Urine is seen in

a. Bilirubinuria
b. Black water fever
c. Melanuria
d. Alkaptonuria
e. All

Q23. Green urine is seen in

a. Bilirubinuria
b. Oxalate poisoning
c. Pneumonia
d. Pleural effusion

Q24. Normal serum cholesterol level is

a. 50 to 150 mg/ 100ml
b. 300 to 350 mg/ 100ml
c. 410 to 560 mg/ 100ml
d. 20 to 30 mg/ 100ml

Q25. Phase I of Xenobiotic reactions include

a. Acetylation
b. Methylatin
c. Hydroxylation
d. Glucorinidation

Q26. Indican in urine is tested by

a. Ehrlich's aldehyde test
b. Obemeyer's test
c. Hay's test
d. Fouchet's test

Q27. Biuret test is mainly done for

a. Carbohydrate
b. Protein
c. Lipids
d. Any of the above

Q28. Benedict's test will be positive in the urine after administration of

a. Folic acid
b. Ascorbic acid
c. Pantothenic acid
d. Retinoic acid

Q29. Siderophillin is

a. Haematin
b. Ferrtin
c. Haemin
d. Transferrin

Q30. The normal value of BUN is

a. 20-40 mg/dl
b. 40-60 mg/dl
c. 8-16 mg/dl
d. 10-20 mg/dl

Q31. In chronic alcoholism the rate limiting component for alcohol metabolism excluding enzymes is/ are

a. NADP
b. NAD+
c. NADPH
d. FADH
e. FAD

15. d	16. a	17. d	18. d	19. b	20. c	21. e	22. b, c, d	23. a
24. a	25. c	26. b	27. b	28. b	29. d	30. d	31. b, c	

Q32. Cholestrol detection can be done with following except

a. Lieberman-burchard reaction
b. Zimmerman reaction
c. Winslow test
d. Salkwski reaction

Q33. Nephelometry is based on the principle of

a. Light attenuated in intensity by scattering
b. Refraction oflight
c. Reduced transmission of light
d. Filtration of solutes by kidney

Q34. On a normal diet, the daily excretion of urea is about

a. 0.5 gm b. 5.0 gm
c. 25.0 gm d. 100.00 gm

Q35. True about G protein coupled receptors is

a. G proteins bind to hormones on the cell surface
b. All the three subunits alpha, beta and gamma should bind to each other for G protein to act
c. G proteins act as inhibitory and excitatory because of difference in alpha subunit
d. G protein is bound tp GTP in resting state

Q36. Following modification occurs in Gs subunit which leads to watery diarrhea in cholera?

a. ADP ribosylation
b. ATP-ADPtransfer
c. Phosphorylation
d. Dephosphorylation

Q37. Green colouration on Benedict's quantitative test implies

a. Negative test
b. Sugar less than 0.5%
c. Sugar between 0.51%
d. Sugar between 12%
e. Sugar over 2%

Q38. Which of the following gives a positive reaction with Ferrous chloride?

a. Phenylketonuria
b. Alkaptonuria
c. Maple syrup urine disease
d. None

Q39. Fluorescamine is used to detect

a. Amino acids b. Fatty acids
c. Glucose d. All

Q40. Positive benzidine test is/are seen in

a. Hemoglobin b. Myoglobin
c. Porphobilinogen d. Glucose
e. Bilirubin

Q41. What is the composition of Lugols solution?

a. 4% iodine 10% potassium iodide
b. 5% iodine and 10% potassium iodide
c. 2.5% iodine and 5% potassium iodide
d. 10% iodine and 6% potassium iodide

Q42. Dietary fibre contain :

a. Collagen b. Pectin
c. Proteoglycans d. Starch

Q43. Not a second messenger

a. cAMP b. cGMP
c. Ca d. G-Protein

Q44. Normal plasma osmolality is:

a. 275-300 milliosmol/ kg
b. 310-340 milliosmol/kg
c. 200-240 milliosmol/kg
d. 160-180 milliosmol/ kg

Q45. The translocation of Ca++ across a membrane :

a. Is a passive mediated transport
b. Is an example of a symptoms system
c. Involves the phosphorylation of a serine residue by ATP
d. May be regulated by the binding of a CA++ calmodulin complex to the transporter

Q46. Which of the following statements about recommended dietary allowances (RDA) is true :

a. RDA is statistically defined as two standard deviations (SD) above estimated average requirement (EAR)
b. RDA is defined as being equal to the estimated average requirement (EAR)
c. RDA is defined as being equal to adequate intake (AI)
d. RDA is defined as the recommended minimum requirement

32. c	33. a	34. c	35. c	36. a	37. b	38. a	39. a	40. a, b	41.b
42. b	43. d	44. a	45. d	46. d					

Miscellaneous – Explanations

1. d) Acts on intrinsic tyrosine kinase receptors

[Ref: Textbook of Medical Biochemistry by Chatterjea and Shinde, 8th edition]

Tyrosine Kinases

Intrinsic tyrosine kinase activity	Extrinsic tyrosine kinase activity
Insulin receptor IGF-1 EGF, PDGF, FGF	Growth hormone Prolactin Erythropoietin Cytokines

	Group I hormones	Group 2 hormones
Solubility	Hydrophobic / lipid soluble	Hydrophilic / water soluble
Types	Steroid hormones Vitamin A and D Thyroid hormones	Polypeptides, proteins Catecholomines
Transport proteins in plasma	YES	No
Receptors	Cytosolic	Membrane bound
Half life	Long (hours to days)	Short (minutes)
Mediator	Hormone receptor dimeric complex	Second messengers
Effect	Days	Minutes to hours

Hormones acting through cytosolic receptors:

Cortisol
Aldosterone
Testosterone
Estrogens
Progesterone

Hormones/vitamins acting through nuclear receptors:

Vitamin A (retinoic acid)
Vitamin D
Thyroid hormone (T3)

Note: All other hormones act through cell membrane receptors.

2. a) Hydroxylation
c) Deamination reaction
d) Involved in hydroxylation of steroids
e) Drug interaction

[Ref: Harper's Illustrated biochemistry, 30th & Lippincott's illustrated reviews, 6th Edition]

Hydroxylation -

Cytochrome P450s are involved in phase I (hydroxylation) of the metabolism of xenobiotics, not in phase II.

Methylation of xenobiotics-

Methylation of xenobiotics occur in phase II by methyl transferase

Deamination reaction –

Reactions Catalyzed by 450:

Aliphatic hydroxylation
Aromatic hydroxylation
N-dealkylation
O-dealkylation
S-demethylation
Epoxidation
Deamination
Sulkfoxide formation
N-oxidation
Dealogenation

Involved in hydroxylation of steroids-

Cytochromes P450 Are Monooxygenases: Important for the Detoxification of Many Drugs and for the Hydroxylation of Steroids.

Drug interaction

Add a note on:

Some properties of human cytochrome P450s:

Involved in phase I of the metabolism of innumerable xenobiotic , Including perhaps 50% of the drugs administered to humans
Involved in the metabolism of many endogenous compound (e.g, steroids)
All are hemoproteins

Often exhibit broad substrate specificity, thus acting on many compounds; consequently, different P450s may catalyze formation of the same product
Extremely versatile catalysts, perhaps catalyzing about 60 types of reactions
However, basically they catalyze reactions involving introduction of one atom of oxygen into the substrate and one into water
Their hydroxylated products are more water-soluble than their generally lipophilic substrates, facilitating excretion
Liver contains highest amounts, but found in most if not all tissues, including small intestine, brain, and lung
Located in the smooth endoplasmic reticulum or in mitochondria (steroidogenic hormones)
In some cases, their products are mutagenic or carcinogenic
Many have a molecular mass of about 55 kDa
Many are inducible, resulting in one cause of drug Interactions
Many are inhibited by various drugs or their metabolic products, providing another cause of drug Interactions
Some exhibit genetic polymorphisms, Which can result in atypical drug metabolism
Their activities may be altered In diseased tissues (e.g, cirrhosis), affecting drug metabolism
Genotyping the P450 profile of patients (e.g, to detect polymorphisms) may in the future permit individualization of drug therapy

3. a) Alcohol dehydrogenase

a. Alcohol dehydrogenase- The active site of alcohol dehydrogenase contains a zinc ion that is coordinated to the sulfur atoms of two cysteine residues and a nitrogen atom of histidine .This zinc ion polarizes the carbonyl group of the substrate to favor the transfer of a hydride from NADH.

b. Pyruvate dehydrogenase –Does not require zinc

c. Pyruvate Decarboxylase- Does not require zinc

d. Alpha keto acid Dehydrogenase- Does not require zinc

4. c) GTP regulating proteins

cAMP-

cAMP-

	cAMP System
First Mesenger: Neuro—transmitters (Receptor)	Epinephrine (α2, β1, β2) Acetylcholine (M2)
First Mesenger: Hormones	ACTH, ANP, CRH, CT, FSH, Glucagon, hCG, Lh, MSH, Pth, TSH
Signal Transducer	GPCR/Gs (β1, β2), Gi (α2, M2)
Primary effector	Adenylyl cyclase
Second messenger	cAMP (cyclic adenosine monophosphate)
Secondary effector	Protein Kinase A

Phosphodiesterase - cAMP is hydrolyzed by phosphodiesterase, so terminating hormone action; in liver insulin increases the activity of phosphodiesterases.

GTP regulating proteins –regulate G Proteins.small GTP ases acts as molecular switches in signaling pathway,which act to regulate functions of other proteins. And are not a part of adenylate cyclase system.

Nuclear receptors - The nuclear receptor superfamily consists of a diverse set of transcription factors that were discovered because of a sequence similarity in their DBDs. This family, now with >50 members, includes the nuclear hormone receptors discussed above, a number of other receptors whose ligands were discovered after the receptors were identified, and many putative or orphan receptors for which a ligand has yet to be discovered. These nuclear receptors have several common structural features .All have a centrally located DBD that allows the receptor to bind with high affinity to a response element. The DBD contains two zinc finger binding motifs that direct binding either as homodimers, as heterodimers (usually with a retinoid X receptor [RXR] partner), or as monomers. The target response element consists of one or two DNA half-site consensus sequences arranged as an inverted or direct repeat. The spacing between the latter helps determine binding specificity.

5. d) Selenium – Dry skin

[Ref: DM Vasudevan, Textbook of Biochemistry for Medical Students, 7th edition]

Explanation:

Folic Acid Deficiency

Reduced DNA synthesis

Macrocytic anemia

Hyperhomocystinemia

Birth defects

Cancer

Deficiency of Iron

Microcytic hypochromic anemia.

Anemia results when hemoglobin level is less than 12 g/dL.

Serum Iron levels reduced, TIBC elevated and Soluble Transferrin receptor levels increased.

Zinc Deficiency

Clinical Features

Poor wound healing

Lesions of skin

Impaired spermatogenesis

Hyperkeratosis

Dermatitis

Alopecia

There is reduction in number of T and B lymphocytes.

Macrophage function is retarded.

Also leads to depression, dementia and other psychiatric disorders.

Selenium Deficiency

In Keshan province in China, the soil is deficient in selenium. This leads to prevalence of Keshan disease.

It is characterized by

Multifocal myocardia necrosis

Cardiac arrhythmias

Cardiac enlargement

Isolated selenium deficiency in other parts of the world caused

Liver necrosis

Cirrhosis

Cardiomyopathy

Muscular dystrophy.

6. d) Amphipathic (amphoteric in nature)

A buffer is a solution that resists change in pH following the addition of an acid or base.

Buffer pairs: The – COOH/– COO– pair can serve as a buffer in the pH region around pK1, and the – NH3+/– NH2 pair can buffer in the region around pK2.

The blood contains 3 buffer systems.

1. Bicarbonate buffer

2. Phosphate buffer

3. Protein buffer.-

Protein buffer system : The plasma proteins and hemoglobin together constitute the protein buffer system of the blood. The buffering capacity of proteins is dependent on the pK of ionizable groups of amino acids. The imidazole group of histidine (pK = 6.7) is the most effective contributor of protein buffers. The plasma proteins account for about 2% of the total buffering capacity of the plasma.

Hemoglobin of RBC is also an important buffer. It mainly buffers the fixed acids, besides being involved in the transport of gases (Oz and CO2). More details on hemoglobin are given under respiratory mechanism for regulation of pH.

7. e) Protein quality

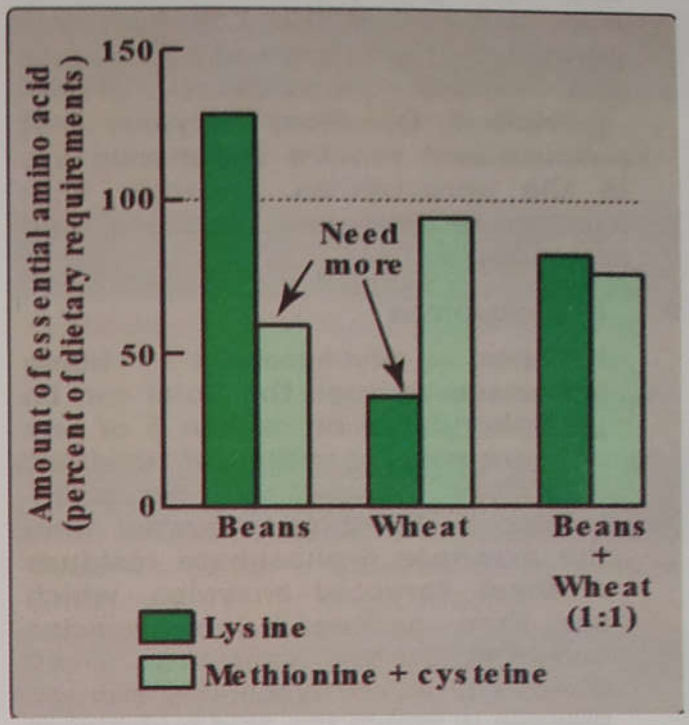
[Ref: Lippincott's illustrated reviews, 6th Edition]

Quality of proteins The quality of a dietary protein is a measure of its ability to provide the essential amino acids required for tissue maintenance. Most government agencies have adopted the Protein Digestibility–Corrected Amino Acid Score (PDCAAS) as the standard by which to evaluate protein quality. PDCAAS is based on the profile of essential amino acids after correcting for the digestibility of the protein. The highest possible score under these guidelines is 1.00. This amino acid score provides a method to balance intakes of poorerquality proteins with high-quality dietary proteins.

proteins from animal sources: Proteins from animal sources (meat, poultry, milk, and fish) have a high quality because they contain all the essential amino acids in proportions similar to those required for synthesis of human tissue proteins ,and they are more readily digested. [Note: Gelatin prepared from animal collagen is an exception. It has a low biologic value as a result of deficiencies in several essential amino acids.]

Source	PDCAAS value
Animal proteins	
Egg	1.00
Milk protein	1.00
Beef/poultry/fish	0.82-0.92
Gelatin	0.08
Plant proteins	
Soybean protein	1.00
Kidney beans	0.68
Whole wheat bread	0.40

2. Proteins from plant sources: Proteins from plant sources have a lower quality than do animal proteins. However, proteins from different plant sources may be combined in such a way that the result is equivalent in nutritional value to animal protein. For example, wheat (lysine deficient but methionine rich) may be combined with kidney beans (methionine poor but lysine rich) to produce an improved biologic value. Therefore, eating foods with different amino acids during the day can result in a dietary combination with a higher biologic value than either of the component proteins. [Note: Animal proteins can also complement the biologic value of plant proteins.]



8. a) Insulin receptors

the insulin receptor is a heterotetramer composed of two copies of two different protein subunits (α2β2) linked by multiple disulfide bonds in which the extracellular α subunit binds insulin and the membrane-spanning β subunit transduces the signal through the tyrosine protein kinase domain located in the cytoplasmic portion of this polypeptide. The receptors for insulin-like growth factor I (IGF-I) and epidermal growth factor (EGF) are generally similar in structure to the insulin receptor. The growth hormone and prolactin receptors also span the plasma membrane of target cells but do not contain intrinsic protein kinase activity. Ligand binding to these receptors, however, results in the association and activation of a completely different protein kinase signaling pathway, the JakStat pathway.

9. b) Peroxisome

Superoxide is produced both accidentally and also as the reactive oxygen species required for a number of enzyme-catalyzed reactions. A family of superoxide dismutases catalyze the reaction between superoxide and water to yield oxygen

and hydrogen peroxide: $O_2^{\cdot -} + H_2O \rightarrow O_2 + H_2O_2$. The hydrogen peroxide is then removed by catalase and various peroxidases: $2H_2O_2 \rightarrow 2H_2O + O_2$. Most enzymes that produce and require superoxide are in the peroxisomes, together with superoxide dismutase, catalase, and peroxidases.

10. b) Lysosomes

N-linked glycoproteins being processed through the Golgi can be phosphorylated on carbon 6 of one or more specific mannosyl residues. Mannose 6-phosphate receptors, located in the Golgi apparatus, bind the mannose 6-phosphate residues of these targeted enzymes, which are then packaged into vesicles and sent to the lysosomes. I-cell disease is a rare lysosomal storage disease in which the acid hydrolases normally found in lysosomes are absent, resulting in an accumulation of substrates normally degraded by these enzymes. [Note: I-cell disease is so-named because of the large inclusion bodies seen in cells of patients with this disease.] In addition, high amounts of lysosomal enzymes are found in the patient's plasma and urine, indicating that the targeting process to lysosomes (rather than the synthetic pathway of these enzymes) is deficient. Individuals with I-cell disease are lacking the phosphotransferase needed to phosphorylate the mannose residues of potential lysosomal enzymes, causing the enzymes to be secreted (by default), rather than being targeted to lysosomal vesicles. I-cell disease is characterized by skeletal abnormalities, restricted joint movement, coarse (dysmorphic) facial features, and severe psychomotor impairment. [Note: Because I-cell disease has features in common with the mucopolysaccharidoses and sphingolipidoses, it is termed a mucolipidosis.] Currently, there is no cure, and death from cardiopulmonary complications usually occurs by age 10 years.

11. a) Basement membrane

Laminin is a major protein component of renal glomerular & other basal laminas.

Basal laminas are specialized areas of the ECM that surround epithelial and some other cells (eg, muscle cells); here we discuss only the laminas found in the renal glomerulus. In that structure, the basal lamina is contributed by two separate sheets of cells (one endothelial and one epithelial), each disposed on opposite sides of the lamina; these three layers make up the glomerular membrane. The primary components of the basal lamina are three proteins—laminin, entactin, and type IV collagen—and the GAG heparin or heparan sulfate. These components are synthesized by the underlying cells. Laminin (about 850 kDa, 70 nm long) consists of three distinct elongated polypeptide chains (A, B1, and B2) linked together to form an elongated cruciform shape . It has potential binding sites for type IV collagen, heparin, and integrins on cell surfaces. The collagen interacts with laminin (rather than directly with the cell surface), which in turn interacts with integrins or other laminin receptor proteins, thus anchoring the lamina to the cells. Entactin, also known as "nidogen," is a glycoprotein containing an RGD sequence; it binds to laminin and is a major cell attachment factor. The relatively thick basal lamina of the renal glomerulus has an important role in glomerular filtration, regulating the passage of large molecules (most plasma proteins) across the glomerulus into the renal tubule. The glomerular membrane allows small molecules, such as inulin (5.2 kDa), to pass through as easily as water.

12. d) GH

[Ref: Harper's Illustrated biochemistry, 28th Edition]

Glycoproteins (also known as mucoproteins) are proteins containing

branched or unbranched oligosaccharide chains ; they occur in cell membranes and many other situations; serum albumin is a glycoprotein. The sialic acids are N- or O-acyl derivatives of neuraminic acid. Neuraminic acid is a nine-carbon sugar derived from mannosamine (an epimer of glucosamine) and pyruvate. Sialic acids are constituents of both glycoproteins and gangliosides.

Many hormones are polypeptides or glycoproteins. These range in size from thyrotropin-releasing hormone (TRH), a tripeptide, to single-chain polypeptides like adrenocorticotropic hormone (ACTH; 39 amino acids), parathyroid hormone (PTH; 84 amino acids), and growth hormone (GH; 191 amino acids). Insulin is an AB chain heterodimer of 21 and 30 amino acids, respectively. Folliclestimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH), and chorionic gonadotropin (CG) are glycoprotein hormones of αβ heterodimeric structure. The α chain is identical in all of these hormones, and distinct β chains impart hormone uniqueness. These hormones have a molecular mass in the range of 25–30 kDa depending on the degree of glycosylation and the length of the β chain.

Angiotensin-converting enzyme, a glycoprotein found in lung, endothelial cells, and plasma, removes two carboxyl terminal amino acids from the decapeptide angiotensin I to form angiotensin II in a step that is not thought to be rate-limiting.

thyroxine-binding globulin (TBG). TBG, a glycoprotein with a molecular mass of 50 kDa, binds T4 and T3 and has the capacity to bind 20 µg/dL of plasma.

Vitamin B12 is absorbed bound to intrinsic factor, a small glycoprotein secreted by the parietal cells of the gastric mucosa.

Function	Glycoproteins
Structural molecule	Collagens
Lubricant and protective agent	Mucins
Transport molecule	Transferrin, ceruloplasmin
Immunologic molecule	Immunoglobulins, histocompatibility antigens
Hormone	Chorionic gonadotropin, thyroid- stimulating hormone [JSH)
Enzyme	Various, eg, alkaline phosphatase
Cell attachment-recognition site	Various proteins involved in cell-cell (eg, sperm-oocyte), virus-cell, bacterium-cell, and hormone-cell interactions
Antifreeze	Certain plasma proteins of cold-water fish
Interact with specific carbohydrates	Lectins, selectins (cell adhesion lectins), antibodies
Receptor	Various proteins involved in hormone and drug action
Affect folding of certain proteins	Calnexin, calreticulin
Regulation of development	Notch and its analogs, key proteins in development
Hemostasis (and thrombosis)	Specific glycoproteins on the surface membranes of platelets

13. a) Growth hormone
c) Insulin
d) Glucagon

The amino acid tyrosine is the starting point in the synthesis of the catecholamines and of the thyroid hormones tetraiodothyronine (thyroxine; T4) and triiodothyronine (T3) . T3 and T4 are unique in that they require the addition of iodine (as I−) for bioactivity. Because dietary iodine is very scarce in many parts of the world, an intricate mechanism for accumulating and retaining I− has evolved. Many hormones are polypeptides or glycoproteins. These range in size from thyrotropin-releasing hormone (TRH), a tripeptide, to single-chain polypeptides like adrenocorticotropic hormone (ACTH; 39 amino acids), parathyroid hormone (PTH; 84 amino acids), and growth hormone (GH; 191 amino acids) . Insulin is an AB chain heterodimer of 21 and 30 amino acids, respectively. Folliclestimulating

hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH), and chorionic gonadotropin (CG) are glycoprotein hormones of αβ heterodimeric structure. The α chain is identical in all of these hormones, and distinct β chains impart hormone uniqueness. These hormones have a molecular mass in the range of 25–30 kDa depending on the degree of glycosylation and the length of the β chain.

14. b) 151-200 mg/L

Microalbuminuria: Microalbuminuria is defined as the excretion of 30-300 mg of albumin in urine per day. It may be noted that microalbuminuria represents an intermediary stage between normal albumin excretion (2.5-30 mg/d) and macroalbuminuria (> 300 mg/d). The small increase in albumin excretion predicts impairment in renal function in diabetic patients. Microalbuminuria serves as a signal of early reversible renal damage.

15. d) Their lipid moieties are amphipathic in nature

a. They are symmetric bileaflet structure-

Membranes Are Asymmetric Structures Proteins have unique orientations in membranes, making the outside surfaces different from the inside surfaces. An inside-outside asymmetry is also provided by the external location of the carbohydrates attached to membrane proteins. In addition, specific proteins are located exclusively on the outsides or insides of membranes, as in the mitochondrial and plasma membranes. There are regional heterogeneities in membranes. Some, such as occur at the villous borders of mucosal cells, are almost macroscopically visible.

b. They constituent lipid & Protein moieties are held together by covalent interaction-

Lipid bilayers are formed by self-assembly, driven by the hydrophobic effect,

THE FLUID MOSAIC MODEL OF MEMBRANE STRUCTURE IS WIDELY ACCEPTED The fluid mosaic model of membrane structure proposed in 1972 by Singer and Nicolsonis now widely accepted. The model is often likened to icebergs (membrane proteins) floating in a sea of predominantly phospholipid molecules.

c. They are rigid assemblies of protein; lipid & carbohydrates-

Membranes Are Dynamic Structures Membranes and their components are dynamic structures. The lipids and proteins in membranes undergo turnover, just as they do in other compartments of the cell. Different lipids have different turnover rates, and the turnover rates of individual species of membrane proteins may vary widely. The membrane itself can turn over even more rapidly than any of its constituents.

d. Their lipid moieties are amphipathic in nature-

Membrane Lipids Are Amphipathic

All major lipids in membranes contain both hydrophobic and hydrophilic regions and are therefore termed amphipathic.

16. a) Cholesterol

The Major Lipids in Mammalian Membranes Are Phospholipids, Glycosphingolipids, & Cholesterol

Phospholipids

Of the two major phospholipid classes present in membranes, phosphoglycerides are the more common and consist of a glycerol backbone to which are attached two fatty acids in ester linkage and a phosphorylated alcohol. The fatty acid constituents are usually even-numbered carbon molecules, most commonly containing 16 or 18 carbons. They are unbranched and can be saturated or unsaturated with one or more cis double bonds. The simplest phosphoglyceride is phosphatidic acid, which is 1,2-diacylglycerol 3-phosphate, a key intermediate in the formation of other phosphoglycerides. In most phosphoglycerides present in membranes, the 3-phosphate is esterified to an alcohol such as ethanolamine,

choline, serine, glycerol, or inositol,The second major class of phospholipids is composed of sphingomyelin, which contains a sphingosine backbone rather than glycerol. A fatty acid is attached by an amide linkage to the amino group of sphingosine, forming ceramide. The primary hydroxyl group of sphingosine is esterified to phosphorylcholine, forming sphingomyelin. As the name implies, sphingomyelin is prominent in myelin sheaths. The amounts and fatty acid compositions of the various phospholipids vary among the different cellular membranes.

Glycosphingolipids The glycosphingolipids (GSLs) are sugar-containing lipids built on a backbone of ceramide; they include galactosyl- and glucosyl-ceramide (cerebrosides) and the gangliosides. They are mainly located in the plasma membranes of cells.

Sterols

The most common sterol in membranes is cholesterol , which resides mainly in the plasma membranes of mammalian cells but can also be found in lesser quantities in mitochondria, Golgi complexes, and nuclear membranes. Cholesterol intercalates among the phospholipids of the membrane, with its hydroxyl group at the aqueous interface and the remainder of the molecule within the leaflet.

17. d) Bicarbonate buffer

A buffer may be defined as a solution of a weak acid (HA) and its salt (BA) with a strong base. The buffer resists the change in pH by the addition of acid or alkali and the buffering capacity is dependent on the absolute concentration of salt and acid. It should be borne in mind that the buffer cannot remove H+ ions from the body. It temporarily acts as a shock absorbant to reduce the free H+ ions. The H+ ions have to be ultimately eliminated by the renal mechanism.

The blood contains 3 buffer systems.

1. Bicarbonate buffer
2. Phosphate buffer
3. Protein buffer

48. d) Involved in carboxylation of drugs

Incorporates one oxygen atom in the substrate

Incorporates two oxygen in the substrate

Involved in hydroxylation reaction

Involved in carboxylation of drugs

OXYGENASES CATALYZE THE DIRECT TRANSFER & INCORPORATION OF OXYGEN INTO A SUBSTRATE MOLECULE

Oxygenases are concerned with the synthesis or degradation of many different types of metabolites. They catalyze the incorporation of oxygen into a substrate molecule in two steps: (1) oxygen is bound to the enzyme at the active site and (2) the bound oxygen is reduced or transferred to the substrate. Oxygenases may be divided into two subgroups, dioxygenases and monooxygenases.

Dioxygenases Incorporate Both Atoms of Molecular Oxygen into the Substrate The basic reaction is shown below:

$A + O_2 \rightarrow AO_2$

Examples include the liver enzymes, homogentisate dioxygenase (oxidase) and 3-hydroxyanthranilate dioxygenase(oxidase), which contain iron; and L-tryptophan dioxygenase (tryptophan pyrolase) , which utilizes heme.

Monooxygenases (Mixed-Function Oxidases, Hydroxylases)

Incorporate Only One Atom of Molecular Oxygen into the Substrate The other oxygen atom is reduced to water, an additional electron donor or cosubstrate (Z) being necessary for this purpose.

$A—H + O_2 + ZH_2 \rightarrow A—OH + H_2O + Z$

Cytochromes P450 Are Monooxygenases Important for the Detoxification of Many Drugs & for the Hydroxylation of Steroids

ADD A NOTE ON:

[Ref: Harper's Illustrated biochemistry, 28th Edition]

Blood Analyte or Measurement	SI Units	Conventional Units
Alanine aminotransferase (ALT)	0.12-0.70 μkat/L	7-41 U/L
Albumin Female Male	 41-53 g/L 40-50 g/L	 4.1 - 5.3 g/dL 4.0 - 5.0 g/dL
Anion gap	7 - 16 mmol/L	7 - 16 mmol/L
Bicarbonate	22 - 30 mmol/L	22 - 30 meq/L
Calcium	2.2 - 2.6 mmol/L	8.7 - 10.2 mg/dL
Carcinoembryonic	0.0 - 3 μg/L	0.0 - 3.0 ng/mL
Antigen (CEA)		
Chloride	102 - 109 mmol/L	102 - 109 meq/L
Cholesterol, total (these levels are considered desirable)	<5.17 mmol/L	<200 mg/dL
Cholesterol, LDL (considered optimal)	<2.59 mmol/L	<100 mg/dL
Cholesterol, HDL	1.03 - 1.55 mmol/L	40 - 60 mg/dL
C-reactive protein	0.20 - 3.0 mg/L	0.20 - 3.0 mg/L
Cretinine Female Male	 44 - 80 μmol/L 55 - 106 μmol/L	 0.5 - 0.9 ng/mL 0.6 - 1.2 ng/mL
Ferritin Female Male	 10 - 150 μg/L 29 - 248 μg/L	 10 - 150 ng/mL 29 - 248 ng/mL
Glucose (fasting)	4.2 - 6.1 mmol/L	75 - 110 mg/dL
Hematocrit Female Male	 0.354 - 0.444 0.388 - 0.464	 35.4 - 44.4 38.8 - 46.4
Hemoglobin Female	120 - 158 g/L	12.0 - 15.8 g/dL

Blood Analyte or Measurement	SI Units	Conventional Units
Iron	7 - 25 μμολ/Λ	41 - 141 μγ/δΛ
Iron-binding capacity	45 - 73 μμολ/Λ	251 - 406 μγ/δΛ
Iron saturation	0.16 - 0.35	16 - 35%
Lactate (arterial blood)	0.5 - 1.6 mmol/L	4.5 14.4 mg/dL
Magnesium	0.62 - 0.95 mmol/L	1.5 - 2.3 mg/dL
Osmolality	275 - 295 mOsmol/kg serum water	275 - 295 mOsmol/kg serum water
PH (arterial)	7.35 - 7.45	7.3 - 7.45
Phosphorus, inorganic	0.81 - 1.4 mmol/L	2.5 - 4.3 mg/dL
Potassium	3.5 - 5.0 mmol/L	3.5- 5.0 meq/L
Protein, total	67 - 86 g/L	6.7 - 8.6 g/dL

Red blood cells Female Male	 4.00 - 5.20 × 10^{12}/L 4.30 - 5.60 × 10^{12}/L	 4.00 - 5.20 × 10^{6}/mm^3 4.30 - 5.60 × 10^{6}/mm^3
Sodium	136 - 146 mmol/L	136 - 146 meq/
Thyroxine Free Total	 10.3 - 21.9 pmol/L 70 - 151 nmol/L	 0.8 - 1.7 ng/dL 5.4 - 11.7 µg/dL
Transferrin	2.0 - 4.0 g/L	200 - 400 mg/dL
Triglycerides (fasting)	0.34 - 2.26 mmol/L	30 - 200 mg/L
Tropornin T	0 - 0.1 µg/L	0 - 0.1 ng/mL
TSH	0.34 - 4.25 miU/L	0.34 - 4.25 µlU/mL
Urea nitrogen	2.5 - 7.1 mmol/L	7 - 20 mg/dL
Uric acid Female	 0.15 - 0.33 mmol/L	 2.5 - 5.6 mg/fL

19. b) Urea cycle

Beta oxidation of fatty acids

Urea cycle

Mitchondria

ETC chain

The orotic aciduria that accompanies Reye syndrome probably is a consequence of the inability of severely damaged mitochondria to utilize carbamoyl phosphate, which then becomes available for cytosolic overproduction of orotic acid.

20. c) Racemization

21. e) All of the above

The Major Lipids in Mammalian Membranes Are Phospholipids, Glycosphingolipids, & Cholesterol

Phospholipids

Of the two major phospholipid classes present in membranes, phosphoglycerides are the more common and consist of a glycerol backbone to which are attached two fatty acids in ester linkage and a phosphorylated alcohol. The fatty acid constituents are usually even-numbered carbon molecules, most commonly containing 16 or 18 carbons.

The second major class of phospholipids is composed of sphingomyelin, which contains a sphingosine backbone rather than glycerol. A fatty acid is attached by an amide linkage to the amino group of sphingosine, forming ceramide. The primary hydroxyl group of sphingosine is esterified to phosphorylcholine, forming sphingomyelin. As the name implies, sphingomyelin is prominent in myelin sheaths. The amounts and fatty acid compositions of the various phospholipids vary among the different cellular membranes.

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Also erythrocyte has Na –K ATPase And Hemoglobin

22. b) Black water fever
c) Melanuria
d) Alkaptonuria

23. a) Bilirubinuria

24. a) 50 to 150 mg/ 100ml

Estimation of serum cholesterol

Serum cholesterol concentration (reference range 150-225 mg/dl) is elevated in atherosclerosis, diabetes mellitus, obstructive jaundice and hypothyroidism. Decreased levels are observed in hyperthyroidism.

Acetic anhydride method: Serum cholesterol reacts with acetic anhydride in the presence of glacial acetic acid and concentrated H2SO4 to form a green coloured complex. Intensity of this colour is measured at 560 nm.

25. c) Hydroxylation

a. Acetylation

b. Methylatin

c. Hydroxylation

d. Glucorinidation

xenobiotic (Gk xenos "stranger") is a compound that is foreign to the body. The principal classes of xenobiotics of medical relevance are drugs, chemical carcinogens, and various compounds that have found their way into our environment by one route or another, such as polychlorinated biphenyls (PCBs) and certain insecticides.

In phase 1, the major reaction involved is hydroxylation, catalyzed mainly by members of a class of enzymes referred to as monooxygenases or cytochrome P450s. Hydroxylation may terminate the action of a drug, though this is not always the case. In addition to hydroxylation, these enzymes catalyze a wide range of reactions, including those involving deamination, dehalogenation, desulfuration, epoxidation, peroxygenation, and reduction. Reactions involving hydrolysis (eg, catalyzed by esterases) and certain other non-P450-catalyzed reactions also occur in phase 1.

In phase 2, the hydroxylated or other compounds produced in phase 1 are converted by specific enzymes to various polar metabolites by conjugation with glucuronic acid, sulfate, acetate, glutathione, or certain amino acids, or by methylation. The overall purpose of the two phases of metabolism of xenobiotics is to increase their water solubility (polarity) and thus excretion from the body.

26. b) Obemeyer's test

a. Ehrlich's aldehyde test

b. Obemeyer's test

c. Hay's test

d. Fouchet's test

27. b) Protein

[Ref: Satyanarayan 4th Edition]

a. Carbohydrate

b. Protein

b. Lipids

d. Any of the above

1. Biuret reactions : Biuret is a compound formed by heating urea to 180'C. When biuret is treatd with dilute copper sulfate in alkaline medium, a purple colour is obtained. This is the basis of biuret test used for identification of proteins and peptides. Biuret test is answered by compounds containing two or more CO-NH groups i.e., pptide funds. All proteins and peptides possessing atleast two peptide linkages i.e., tripeptides (with 3 amino acids) give positive biuret test. The principle of biuret test is conveniently used to detect the presence of proteins in biological fluids. The mechanism of biuret test is not clearly known. It is believed that the colour is due to the formation of a copper co-ordinated complex.

Ninhydrin reaction: The cr-amino acids react with ninhydrin to form a purple, blue or pink colour complex (Ruhemann's purple).

Xanthoproteic reaction r Xanthoproteic reaction is due to nitration oI aromatic amino acids (tryptophan, tyrosine and phenylalanine) on treatment with strong nitric acid at high temperature.

Millon's test: This test is given by the amino acid tyrosine, or any other compound containing hydroxyphenyl ring. A red colour or precipitate is obtained in this reaction due to the formation of mercury complex of nitrophenol derivative.

Hopkins'Cole reaction: This reaction is specific for the indole ring of tryptophan It combines with formaldehyde in the presence of the oxidizing agent (sulfuric acid with mercuric sulfate) to form a violet or purple coloured compound.

Sakaguchi reaction: Arginine, containing guanidino group, reacts with a-naphthol and alkaline hypobromite to form a red colour complex.

Sulfur test: This is a test specific for sulfur containing amino acids namely cydeine and cystine, but not methionine. When cysteine and cystine are boiled with sodium hydroxide, organic sulfur is converted to inorganic sodium sulfide. This reacts with lead acetate to form a black precipitate of lead sulfide. Methionine does not give this test, since sulfur of methionine is not split by alkali.

Pauly/s test : This reaction is specific for histidine (imidazole ring). Diazotised sulfanilic acid reacts with imidazole ring in alkaline medium to form a red coloured complex.

Molisch test : This is a specific test for the detection of carbohydrafes. The proteins containing carbohydrates (e.9., glycoproteins) give this test positive. Albumin contains carbohydrate bound to it, hence answers Molisch test.

Reaction	Specific group or ammo acid
1. Biuret reaction	Two peptide linkages
2. Ninhydrin reaction	α-Amino acids
3. Xanthoproteic reaction	Benzene ring of aromatic amino acids (Phe, Tyr, Trp)
4. Millons reaction	Phenolic group (Tyr)
5. Hopkins-Cole reaction	Indole ring (Trp)
6. Sakaguchi reaction	Guanidino group (Arg)
7. Nitroprusside reaction	Sulfhydryl groups (Cys)
8. Sulfur test	Sulfhydryl groups (Cys)
9. Paul/stest	Imidazole ring (His)
10. Folin-Coicalteau's test	Phenolic groups (Tyr)

28. b) Ascorbic acid

[Ref: Satyanarayan 4th Edition]

Benedict's test: This is a test for the identification of reducing sugars, which form enediols (predominantly under alkaline conditions). The enediol forms of sugars reduce cupric ions (Cu2+) of copper sulfate to cuprous ions (Cu+) which form a yellow precipitate of cuprous hydroxide or a red precipitate of cuprous oxide.

29. d) Transferrin

siderophilin - a globulin in blood plasma that carries iron. beta globulin, transferrin. globulin - a family of proteins found in blood and milk and muscle and in plant seed.

30. d) 10-20 mg/dl

In healthy persons, NPN concentration in blood is 20-4O mg/dl. The molecular weight of urea is 60 and about half of it (28) is contributed by the two nitrogen atoms. Thus, if blood urea concentration is 60 mg, then about half of it-28 mg-is blood urea nitrogen (BU N).

31. b) NAD+
c) NADPH

a. NADP **b. NAD+**
c. NADPH **d. FADH**
e. FAD

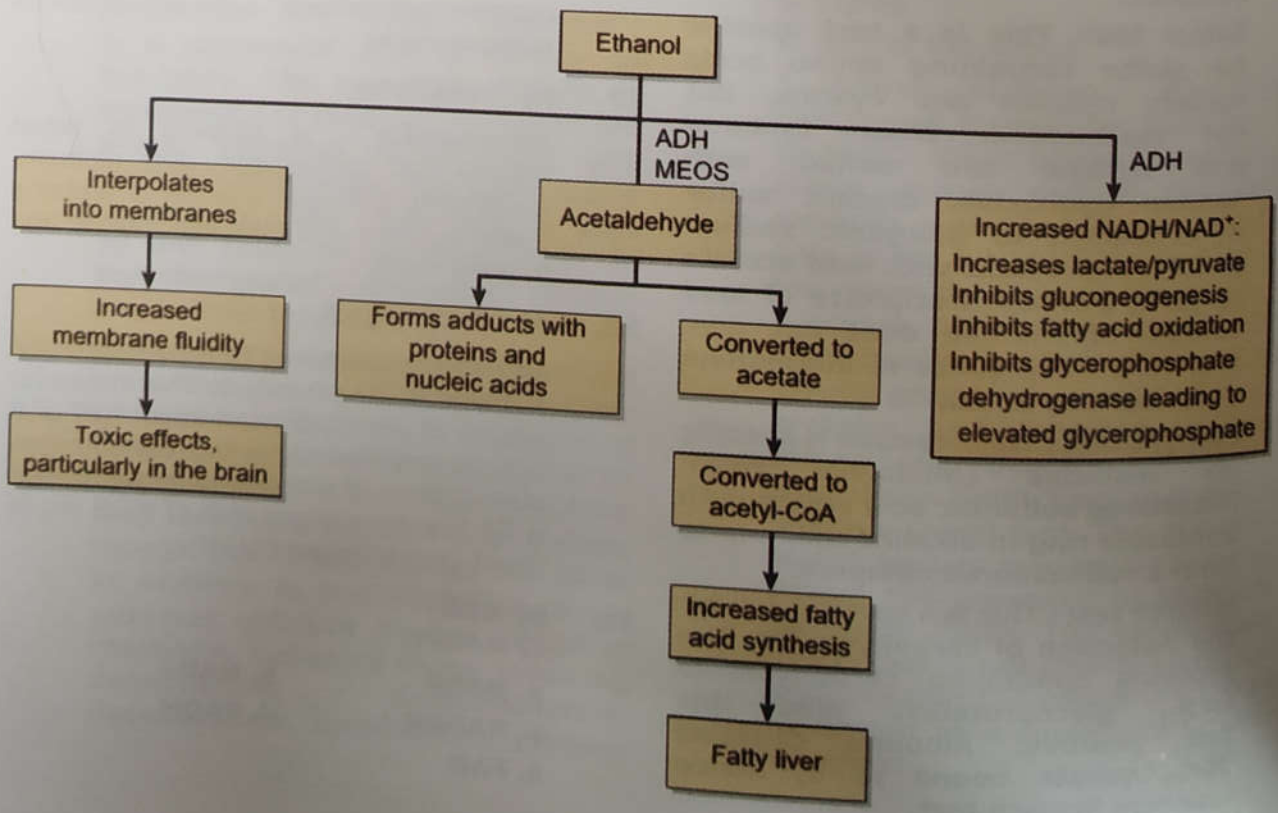
Excessive consumption of alcohol is a major health problem in most societies. The present case deals with the acute, toxic effects of a very large intake of ethanol.

The metabolism of ethanol occurs mainly in the liver and involves two routes. The first and major route uses alcohol dehydrogenase and acetaldehyde dehydrogenase, converting ethanol via acetadehyde to acetate, which is then converted to acetyl-CoA.

The intracellular ratio of NADH/NAD+ can thus be increased appreciably by ingestion of large amounts of ethanol.

In turn, this can affect the Keq of a number of important metabolic reactions that use these two cofactors. High levels of NADH favor formation of lactate from pyruvate, accounting for the lacticacidosis. This diminishes the concentration of pyruvate and thus inhibits gluconeogenesis.

In severe cases, when liver glycogen is depleted and no longer available for glycogenolysis, hypoglycemia results. The second route involves a microsomal cytochrome P450 (microsomal ethanol oxidizing system), also producing acetaldehyde . Acetaldehyde is a highly reactive molecule and can form adducts with proteins, nucleic acids, and other molecules. It appears likely that its ability to react with various molecules is involved in the causation of the toxic effects of ethanol. Ethanol also appears to be able to interpolate into biologic membranes, expanding them and increasing their fluidity. When the membranes affected are excitable, this results in alterations of their action potentials, impairs active transport across them, and also affects neurotransmitter release. All of these depress cerebral function and, if severe enough, can produce coma and death from respiratory paralysis.



Summarizes some of the major mechanisms

involved in the causation of toxicity by ethanol.

32. c) Winslow test

Cholesterol is yellowish crystalline solid. Cholesterol is insoluble in water and soluble in organic solvents such as chloroform, benzene, ether etc.

Several reactions given by cholesterol are useful for its qualitative identification and quantitative estimation. These include

Salkowski's test,

Liebermann-Burchard reaction

Zak's test

33. a) Light attenuated in intensity by scattering

Nephelometry is concerned with measurement of scattered light from a cuvette containing suspended particles in a solution. The components of a **nephelometer** are the same as a light spectrophotometer except that the detector is placed at a specific angle from the incident light.

34. c) 25.0 gm

a. 0.5 gm

b. 5.0 gm

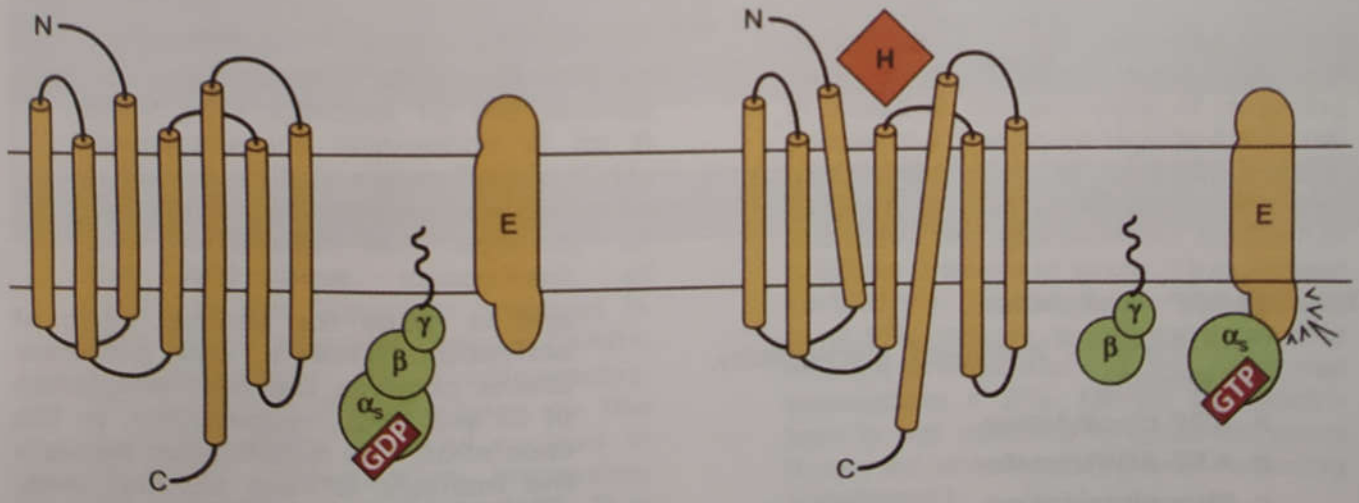
c. 25.0 gm

d. 100.00 gm

35. c) G proteins act as inhibitory and excitatory because of difference in alpha subunit

[Ref: Harper's Illustrated biochemistry, 28th Edition]

G Protein–Coupled Receptors (GPCR) Many of the group II hormones bind to receptors that couple to effectors through a GTP-binding protein intermediary. These receptors typically have seven hydrophobic plasma membrane-spanning domains. This is illustrated by the seven interconnected cylinders extending through the lipid bilayer in



No hormone: inactive effector

Bound hormone (H): active effector

Receptors of this class, which signal through guanine nucleotide-bound protein intermediates, are known as G protein–coupled receptors, or GPCRs. To date, hundreds of G protein–linked receptor genes have been identified; this represents the largest family of cell surface receptors in humans. A wide variety of responses are mediated by the GPCRs.

cAMP Is the Intracellular Signal for Many Responses Cyclic AMP was the first intracellular signal identified in mammalian cells. Several components comprise a system for the generation, degradation, and action of cAMP.

Adenylyl Cyclase Different peptide hormones can either stimulate (s) or inhibit (i) the production of cAMP from adenylyl cyclase, which is encoded by at least nine different genes. Two parallel systems, a stimulatory (s) one and an inhibitory (i) one, converge upon a catalytic molecule (C).

Class or Type	Stimulus	Effector	Effect
G_s			
α_s α_{olf}	Glucagon, β-adrenergics	↑ Adenylylcyclase ↑ Cardiac Ca^{2+}, Cl^-, and Na^+ channels ↑ Adenylyl cyclase	Glyconeogenesis, lipolysis, glycogenolysis Olfaction
G_i			
$\alpha_{i-1,2,3}$ α_0 α_t	Acetylcholine, α_2-adrenergics M_2 cholinergics Opioids, endorphins Light	↓ Adenylyl cyclase ↑ Potassium channels ↓ Calcium channels ↑ Potassium channels ↑ cGMP phosphodiesterase	Slowed heart rate Neuronal electrical activity Vision
G_q			
α_q α_{11}	M_1 cholinergics α_1 - Adrenergics α_1 - Adrenergics	↑ Phospholipase C-β1 ↑ Phospholipase C-β2	↓ Muscle contration and ↓ Blood pressure
G_{12}			
α_{12}	?	Cl channel	?

36:. a) ADP ribosylation

[Ref: Harper's Illustrated biochemistry, 28th Edition]

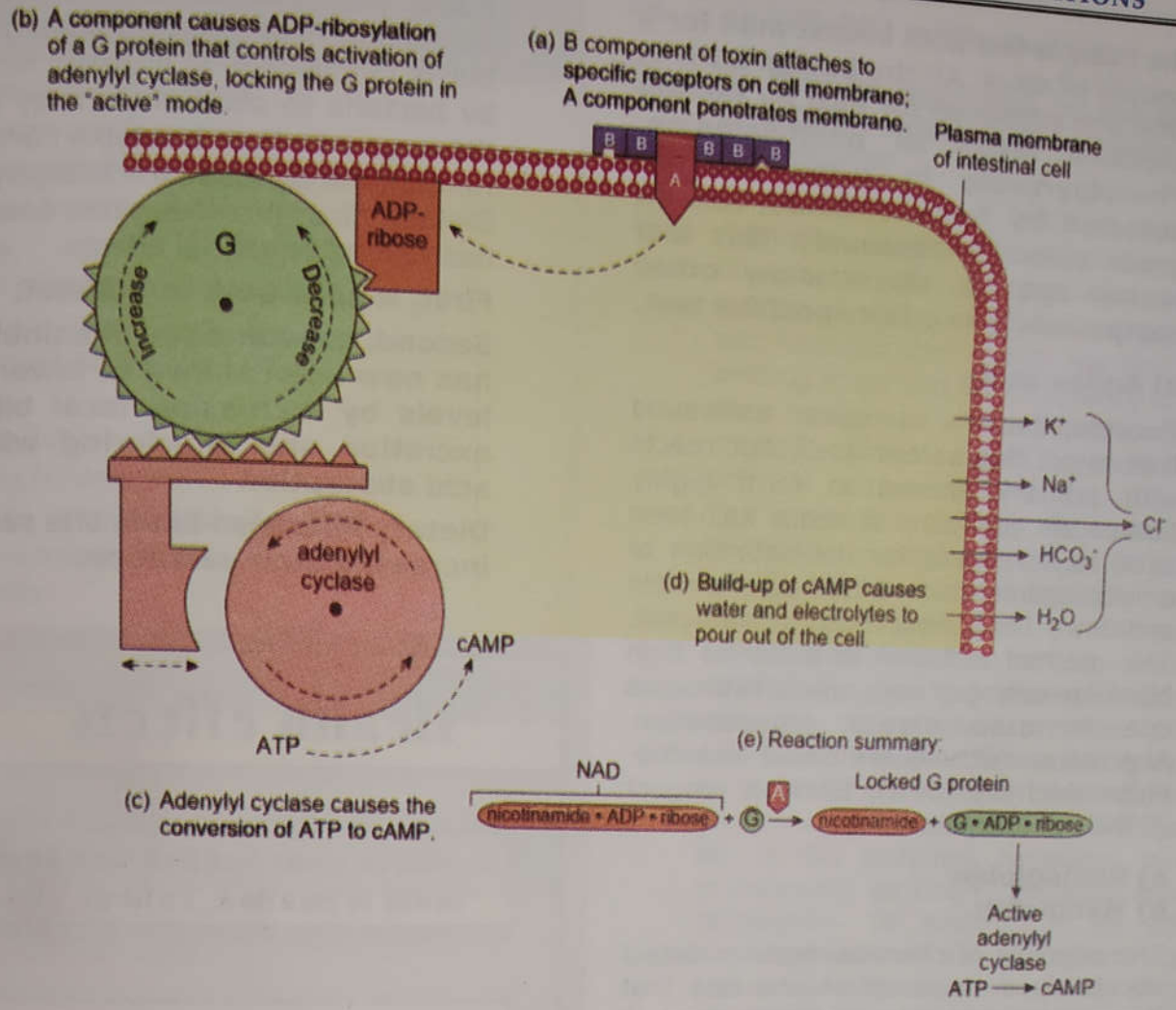
a. ADP ribosylation

b. ATP-ADPtransfer

c. Phosphorylation

d. Dephosphorylation

The αs protein has intrinsic GTPase activity. The active form, αs·GTP, is inactivated upon hydrolysis of the GTP to GDP; the trimeric Gs complex (αβγ) is then re-formed and is ready for another cycle of activation. Cholera and pertussis toxins catalyze the ADPribosylation of αs and αi-2 , respectively. In the case of αs, this modification disrupts the intrinsic GTPase activity; thus, αs cannot reassociate with βγ and is therefore irreversibly activated. ADP ribosylation of αi-2 prevents the dissociation of αi-2 from βγ, and free αi-2 thus cannot be formed. αs activity in such cells is therefore unopposed.


(b) A component causes ADP-ribosylation of a G protein that controls activation of adenylyl cyclase, locking the G protein in the "active" mode.
(a) B component of toxin attaches to specific receptors on cell membrane; A component penetrates membrane.
Plasma membrane of intestinal cell
B B B B B
A
ADP-ribose
G
Increase
Decrease
adenylyl cyclase
cAMP
ATP
(c) Adenylyl cyclase causes the conversion of ATP to cAMP.
K+
Na+
Cl-
HCO3-
H2O
(d) Build-up of cAMP causes water and electrolytes to pour out of the cell.
(e) Reaction summary:
NAD
nicotinamide • ADP • ribose
+ G
A
Locked G protein
nicotinamide + G • ADP • ribose
Active adenylyl cyclase
ATP → cAMP

Diagrammatic representation of the mechanism of action of cholera toxin (CT) attaches to the plasma membrane via interaction of its B subunits with the ganglioside GM1. The A subunit crosses the membrane and catalyzes the addition of the ADP-ribose component of NAD+ to the G protein involved in stimulating adenylyl cyclase (NAD+ → ADP-ribose + nicotinamide). The addition of ADP-ribose to the G protein locks adenylyl cyclase in its active conformation, increasing the intracellular level of cAMP. This leads to phosphorylation of several membrane transporters, in turn resulting in accumulation of the ions shown and of water in the intestinal lumen, thus producing often massive diarrhea.

37. b) Sugar less than 0.5%

Benedict's tegt: This is a semiquantitative test for the detection of urine reducing sugars (primarily glucose). Benedict's test is based on the principle of reducing property of sugars (described in detail under reactions of carbohydrates). Colour of the precipitate formed indicates the approximate amount of glucose present in urine. Thus, green turbidity = traces; Breen precipitate = O.5% yellow precipitate = 1%; orange precipitate = 1.5% brick red precipitate = 2%. (Note: Benedict's test is not specific to glucose, since it can be answered by any reducing substance).

38. a) Phenylketonuria

PKU is mostly detected by screening the newborn babies for the increased plasma levels of phenylalanine (PKU, 20-65 mg/ dl; normal 1-2mg/dl). This is usually carried out by Guthrie fest, which is a bacterial (Bacillus subtilis) bioassay for phenylalanine. The test is usually performed after

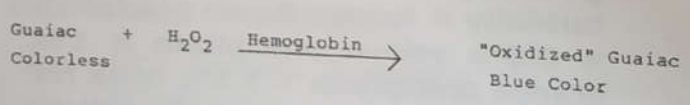
the baby is fed with breast milk for a couple of days. All the babies born in USA are screened for PKU by testing elevated levels of phenylalanine. Phenylpyruvate in urine can be detected by ferric chloride test (a green colour is obtained). This test is not specific, since many other compounds give a false positive test.

39. a) Amino acids

Fluorescamine is a spiro compound that is not fluorescent itself, but reacts with primary amines to form highly fluorescent products. It hence has been used as a reagent for the detection of amines and peptides. 1-100 µg of protein and down 10pg protein can be detected. This method is found to suffer of high blanks resulting of high rate of hydrolysis due to used excess concentration. Alternative methods are based on ortho-Phthalaldehyde (OPA), Ellman's reagent (DTNB) and epicocconone.

40. a) Hemoglobin
b) Myoglobin

The principle of chemical tests to detect occult blood is based on the fact that hemoglobin and its derivatives react in a similar way to **peroxidase enzymes**– by catalyzing the transfer of an oxygen atom from the peroxide to a chromogen such as **benzidine, o-toludine, guaiac or aminophenazone**. Oxidation of the chromogen is indicated by the production of a **blue, blue-green** or **pink** color. A simplified reaction equation is shown below:



41. b) 5% iodine and 10% potassium iodide

42: b) Pectin

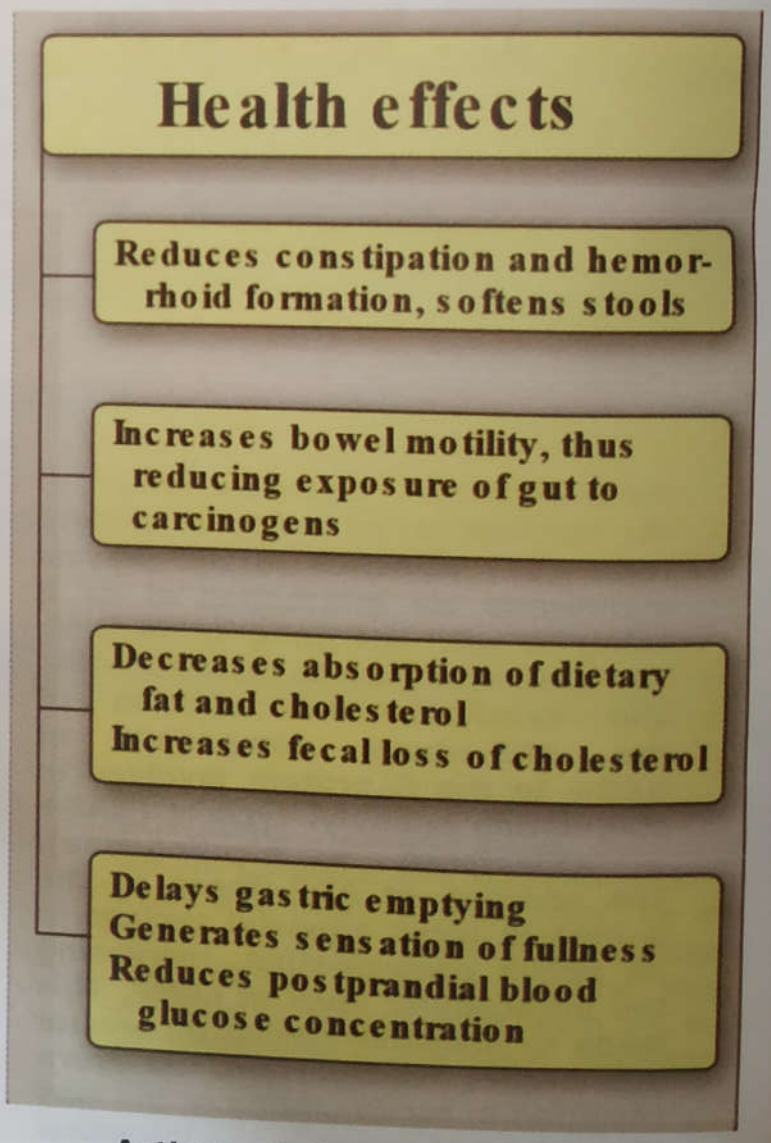
[Ref: Lippincott's illustrated reviews, 6th Edition]

Fiber: Dietary fiber is defined as the nondigestible, nonstarch carbohydrates and lignin (a noncarbohydrate polymer of aromatic alcohols) present intact in plants. Soluble fiber is the edible parts of plants that is resistant to digestion and absorption in the human small intestine but is completely or partially fermented by bacteria to short-chain fatty acids in the large intestine. Insoluble fiber passes through the digestive track largely intact. Dietary fiber provides little energy but has several beneficial effects.

First, it adds bulk to the diet.

Second, consumption of soluble fiber has now been shown to lower LDL-C levels by increasing fecal bile acid excretion and interfering with bile acid absorption .

Dietary fiber also binds bile salts and increases their excretion.


Health effects
Reduces constipation and hemorrhoid formation, softens stools
Increases bowel motility, thus reducing exposure of gut to carcinogens
Decreases absorption of dietary fat and cholesterol
Increases fecal loss of cholesterol
Delays gastric emptying
Generates sensation of fullness
Reduces postprandial blood glucose concentration

Actions of dietary fiber.

43. d) G-Protein

[Ref: Harper's Illustrated biochemistry, 28th Edition]

II. Hormones that bind to cell surface receptors A. The second messanger is cAMP
α_2-Adrenergic catecholamines
β- Adrenergic catecholamines
Adernocorticotropic hormone (ACTH)
Antidiuretic hormone
Calcitonin
Chorionic gonadotropin, human (CG)
Corticotropin releasing hormone
Follicle-stimulating hormone (FSH)
Glucagon
Lipotropin (LPH)
Luteinizing hormone (LH)
Melanocyte- stimulating hormone (MSH)
Parathyroid hormone (PTH)
Somatostatin
Thyroid- stimulating hormone (TSH)
B. The second messanger is cGMP
Antiral natriuretic factor
Nitric oxide
C. The second messanger in calcium or phosphatidylinositols (or both)
Acetylcholine (muscarinic)
α_1- Adrenergic catecholamines
Angiotensin II
Antidiuretic hormone (vasopressin)
Cholecystokinin
Gastrin
Gonadotropin - releasing hormone
Oxytocin
Platelet - derived growth factor (PDGF)
Substance P
Thyrotropin - releasing hormone (TRH)
D. The second messanger is a kinase or phosphatase cascade
Adiponectin
Chorionic somatomammotropin
Epidermal growth factor
Erythropoietin
Fibroblast growth factor (FGF)
Growth hormone (GH)
Insulin
Insulin-like growth facotrs I and II
Leptin
Nerve growth factor (NGF)
Platelet - derived growth factor
Prolactin

44. a) 275-300 milliosmol/ kg

45. d) May be regulated by the binding of a CA++ calmodulin complex to the transporter

Calmodulin The calcium-dependent regulatory protein is calmodulin, a 17-kDa protein that is homologous to the muscle protein troponin C in structure and function. Calmodulin has four Ca2+ binding sites, and full occupancy of these sites leads to a marked conformational change, which allows calmodulin to activate enzymes and ion channels. The interaction of Ca2+ with calmodulin (with the resultant change of activity of the latter) is conceptually similar to the binding of cAMP to PKA and the subsequent activation of this molecule. Calmodulin can be one of numerous subunits of complex proteins and is particularly involved in regulating various kinases and enzymes of cyclic nucleotide generation and degradation. A partial list of the enzymes regulated directly or indirectly by Ca2+, probably through calmodulin. In addition to its effects on enzymes and ion transport, Ca2+/ calmodulin regulates the activity of many structural elements in cells. These include the actin-myosin complex of smooth muscle, which is under β-adrenergic control, and various microfilament-mediated processes in noncontractile cells, including cell motility, cell conformation changes, mitosis, granule release, and endocytosis.

46. d) RDA is defined as the recommended minimum requirement

Recommended Dietary Allowance: The RDA is the average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97%–98%) individuals in a life stage and gender group. The RDA is not the minimal requirement for healthy individuals, but it is intentionally set to provide a margin of safety for most individuals. The EAR serves as the foundation for setting the RDA. If the standard deviation (SD) of the EAR is available and the requirement for the nutrient is normally distributed, the RDA is set at 2 SDs above the EAR (that is, RDA = EAR + 2SDEAR).